LECTURES ON THE SCIENTIFIC BASIS OF MEDICINE
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PREFACE

THE series of lectures on the Scientific Basis of Medicine arranged each year by the British Postgraduate Medical Federation continue to attract appreciative audiences and comments and the Governing Body of the Federation believes that the publication of an annual volume containing the majority of the lectures in each series is of considerable value Without the ready co-operation of the experts all actively engaged in research who accept the invitations to contribute, this venture in postgraduate education would not be possible and the Governing Body is grateful to them The lectures are designed to illustrate the new methods being used to advance knowledge in the sciences on which the practice of medicine is based and to indicate where progress and new knowledge are being developed They are intended for graduates in medicine *looking forward to careers as teachers and consultants in* medicine and surgery and their special branches as well as for those seeking careers in research and teaching in the medical sciences This volume the seventh in the series includes twenty three of the twenty nine lectures delivered during the winter of 1957–58

Most of the lectures in this volume exemplify the numerous investigations now being made of the smaller biological units, the cells and the structures that compose them, and the functions of these small units These investigations require the use of a variety of methods and disciplines Studies in cytology are illustrated by the lectures of Payling Wright on cell regeneration in liver parenchyma of L H Gray on the influence of oxgyen on the response of cells and tissues to ionizing radiations, of Rees on the experimental approach to the problem of resistance to tuberculosis of Yoffey on some of the problems of lymphoid tissues, and of Stoker on the growth of viruses The results of the

use of micro electric methods in the investigation of the functions of cells in the nervous system are reported by Gordon in his lecture on psychological problems in the central pathway for somatic and visceral sensation and by J A B Gray on peripheral mechanisms responsible for sensations and studies on the nervous control of cells are reported by Edith Bulbring in her lecture on the physiology and pharmacology of intestinal smooth muscle The use of microchemical methods is illustrated by Hallpike s lecture on the scientific basis of otological practice in which he reports his investigations on the nature of the endolymph by Fourman s lecture on potassium deficiency, and Glynn s on the structure and stability of collagen in diseases of connective tissue

The study of genetics is throwing new light on many problems and this is well represented by Penrose in his lecture on biochemical genetics in medicine, by Fraser Roberts on blood group genetics and by Rosemary Biggs on haemophilia and Christmas disease Studies on other haematological disorders by a variety of methods are seen in the lecture by Dacie on acquired haemolytic anaemia which deals especially with the phenomenon of auto-antibodies, and in that by Mollin on the megaloblastic anaemias and the utilization of folic acid Other metabolic studies are those by Cross on anoxia of the new born and by Humphrey on the metabolism of gamma globulins, a subject of fundamental importance in antibody formation and resistance to infection

Lectures on subjects of current interest are those by Montgomery on problems in the pathology of coronary artery disease by Peart on biochemical aspects of hypertension and by Dick dealing with the epidemiological problems of poliomyelitis The lecture by Krohn on the processes of ageing in the reproductive system illustrates the growing importance of community medicine and studies of populations and the lecture by Shillingford on the study of the circulation by dye dilution curves will be of interest to the many concerned with the investigation of the cardiovascular systems of their patients

Volume VIII of this series based on the lectures delivered during the winter of 1958–59 is now in the course of preparation

by the Athlone Press and will include further contributions in the fields of cytology, genetics, biochemistry and cardiovascular disorders

FRANCIS R. FRASER
Director, British Postgraduate Medical Federation

30 *April* 1959

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NOTE

The lectures printed in this volume were delivered on the following dates

I	6 February 1958	XII	21 November 1957
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XXIII 29 October 1957

I

Some Remarks upon the Scientific Basis of Otological Practice

C S HALLPIKE

During the last two decades the chemical control of bac teria has made it possible for the otologist to transfer at least part of his energies and interests from the middle ear and its infections to the more complex problems of the labyrinth and its central connexions The subject is a large one and what I have to say can comprise but a part of it, namely those lines of clinical and laboratory work which come within the direct experience of my associates and myself at Queen Square

Fluid System of Inner Ear

I propose to begin with a brief and elementary review of the fluid system of the inner ear This is shown in a highly simplified form in Figure 1 The walls of the bony labyrinth are shown in black On the outer wall are the oval window above occupied by the stapes footplate, and below, the round window occupied by a thin elastic membrane The space within is filled with fluid the perilymph which reaches it in part from the subarachnoid space of the posterior fossa by way of the cochlear aqueduct This aqueduct varies greatly in length and diameter from species to species and in many the fluid ex changes through it must be very slow In fact although we may still be correct in regarding the perilymph space as a sort of diverticulum or backwater of the subarachnoid space, in some species and this includes man, it is a comparatively tideless one Immersed within this bath of perilymph lies the closed

thin walled sac of the endolymph system, filled with a fluid of its own, the endolymph, and bearing on its walls the sense organs of hearing and equilibrium, and a gland like structure, the stria vascularis In Plate I, Figure 2, is shown the system in its true

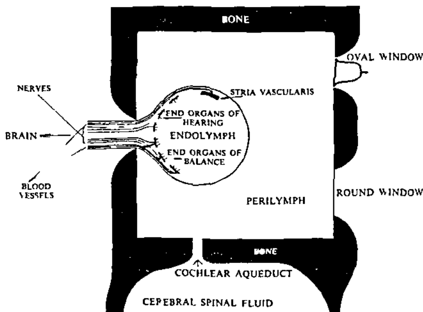


FIGURE 1 The fluid system of the mammalian labyrinth Schematic

form [1] The endolymph system is shown in black Anteriorly is seen the coil of the cochlear portion, posteriorly the sacs of the saccule and utricle with the semicircular canals finally, the ductus endolymphaticus leading to the saccus endolymphaticus lying in the dura mater on the posterior aspect of the temporal bone Surrounding the endolymph system the perilymph spaces are shown in white, with the oval and round windows and the cochlear aqueduct connecting the basal coil of the cochlea to the subarachnoid space

We come next to the problem of the endolymph itself its function, origin, circulation and composition A well known

[1] The plates referred to in this lecture will be found between pages 8–9

structural feature of Corti's organ is the absence therefrom of blood capillaries, and this has led to the widely held belief that the endolymph is a rather special fluid with a rather special function, namely, the maintenance of the metabolic processes of Corti s organ As the probable source of the endolymph, much has been made of the stria vascularis, partly because of its proximity to the organ of Corti, partly because of its vascularity and the histological character of its cells

In Plate I, Figure 3, is shown the stria of a young mouse, and in it can be seen many of the features so well described by Shambaugh in 1908 the richly staining and striated cytoplasm of the cells with their abundant granules, the large vascular spaces and intercellular interstices—all of which led him to believe that the endolymph was a secretory product of the stria

Suggestive as it was, this evidence was only circumstantial Something more direct was required, and this was provided by the experimental work of Guild in 1927, who endeavoured to trace the flow of the endolymph from the scala media by means of the Prussian blue granule technique For this purpose he injected the iron salt solutions into the scala media of the guinea pig s cochlea through a small hole drilled in its bony wall The animals were killed at varying periods following this procedure and a histological study made of the distribution of the granules within and around the labyrinth

Guild s results and conclusions are summarized in Plate II, Figure 4 The granule distribution showed a rapid fluid flow from the scala media into the saccule and thence into the saccus endolymphaticus, and through its walls into the loose perisaccal connective tissue From there he concluded that it was absorbed into the radicles of the neighbouring great venous sinuses This was the position as Guild left it His experiments were difficult ones It was difficult to perform them, at least as difficult to interpret their results, and so far as I know they have never been repeated Although not decisive they nevertheless focused attention upon a conundrum which has held the attention of clinicians for more than a century namely, the pathological mechanism of Menière s disease of the labyrinth In the last two decades we have seen good progress towards its solution a clear

picture of its morbid anatomy has been established, and as a result, the various derangements of hearing and equilibrium so characteristic of the disorder have become explicable upon a clear anatomical basis Existing functional tests have thus acquired new values, others, more rational and penetrating, have been developed In this way the clinical features of the disease itself have acquired much sharper outlines and its diagnosis, sometimes very difficult from allied disorders of the viii nerve system, has been greatly clarified

Ménière s Disease

Something, though not a great deal, needs to be said of Menière himself and his work Although Flouren's experimental work on pigeons, in which he first demonstrated the gross disorders of equilibrium which could result from injuries of the semi circular canals had been published in 1820, some forty years before the publication of Menière s best known paper, its bearing upon the problem of human vertigo was not at first widely appreciated, and indeed, the very possibility that a lesion of the inner ear could cause severe vertigo and vomiting was slow to gain acceptance It was Menière s great merit that he knew of Flouren s work, understood its meaning, and was thus able to ascribe to a labyrinthine lesion the disorder, so spec tacular and distressing, which has since come to bear his name

Its clinical features he described with great precision the paroxysmal character of the attacks with their paralysing vertigo, nausea and vomiting so characteristically accompanied by exacerbations of deafness and tinnitus He made much, too of the natural history of the disease its benign character, benign that is to say in that it did not appear to shorten life and the absence of collateral evidence of any serious disease of the cen tral nervous system and from an analysis of this clinical pic ture he correctly inferred that the underlying lesion was to be found in the semicircular canals

As to the nature of the lesion, this problem he left unsolved, and so it was to remain until 1938 when the first of a series of histological examinations of the temporal bones of affected subjects at last gave us a clear picture of its micro anatomy

In Plate II Figure 5, is shown a transverse section of the unaffected temporal bone of a subject of Menière s disease

In Plate II, Figure 6 is shown a corresponding view of the affected temporal bone Here in the vestibule, the saccule is distended, its membrane being pushed back everywhere on to the bony vestibular wall with obliteration of the perilymph space which lies deep to the stapes footplate In the cochlea the outstanding abnormality is the apparent disappearance of Reissner s membrane In fact, this disappearance is brought about by gross distension of the scala media with displacement of the membrane on to the bony wall of the scala vestibuli

In Plate III Figure 7, is shown the unaffected cochlea at a higher magnification No abnormality can be seen in the fibres of the cochlear nerve as they lie in the spiral osseous lamina, while the cells of the spiral ganglion are also normal in number and structure In Plate III, Figure 8, is shown a corresponding view of the affected cochlea with distension of the scala media It shows, too, certain changes in the cells of Corti s organ, which are displayed at a higher magnification in Plate IV, Figure 9

Above (*a*) is shown Corti s organ of the unaffected ear with its hair cells and Corti s rods enclosing a well formed tunnel Below (*b*) on the affected side, the whole mass of Corti s organ is greatly compressed and its outlines irregular, while Corti s tunnel is occupied by a structureless coagulum

Changes closely resembling these have now been found by a number of observers in the temporal bones of a considerable number of subjects with Menieres disease and it is safe to describe them as constituting its essential morbid anatomy As to the cause of the endolymphatic distension little even now, can be said Some evidence mainly histological has been advanced for a primary failure of the absorptive mechanism of the endolymphatic sac This evidence, however is far from strong and the alternative possibility of some defect qualitative or quantitative, of the endolymph itself has attracted much attention attention which has been much stimulated by recent developments in the field of microchemical analysis This work though still in its early stages has already revealed for the endo lymph a chemical constitution which marks it as one of the most

LIST OF ILLUSTRATIONS

Chapter One

AGING AND DISEASE

AT THE beginning of the twentieth centur
cent of our population were over 65 and 18 p
45 years of age or older today 6 8 per cent
27 per cent are 45 years of age or older In the U
there now are actually 6 000 000 more pers
years of age or older than there were in 19
mated that by 1980 the total number of th
group will be 22 000 000 Two importa
population trend are the marked fall in the
has dropped more than a third in the past
sharp drop in immigration of young adults

At the same time there has been a great
mean life span that is in the average expec
birth At the time of the American Revol
length of life was 35 5 years by 1900 it had
and today it is over 65 years This extension
life span is due largely to the reduction in th
eases in infancy and childhood and in earl
reduction in death rates has taken place
viduals below the age of 50 but there has
saving of life in the older age groups With
tion in the ravages of the acute infectious dis
been a steady increase in frequency of the

which today are responsible for three quarters of all deaths This increasing prevalence of certain chronic diseases such as arteriosclerosis and hypertension has been ascribed to the strain and stress of our complex modern civilization Unprejudiced study however demonstrates that the increasing prevalence of chronic diseases is due to beneficent rather than to malign forces We are spared attack by the infectious diseases in our younger years and survive to succumb at a more advanced age to one of the chronic diseases Over 60 per cent of all deaths now occur after the age of 45 The physician is called on to treat more and more older patients suffering from one of the chronic diseases

Cardiovascular renal diseases are the most frequent of all the chronic diseases In the decade 50 to 59 they are responsible for 40 per cent of all deaths Their frequency increases with each succeeding year of life and in the decade 80 to 89 they cause two thirds of all deaths Among the other chief causes of death in persons past 50 years of age are cancer 12 per cent accidents 8 per cent influenza and pneumonia 7 per cent tuberculosis and diabetes There are other diseases common among older persons that cause much illness and disability but rarely appear as direct causes of death Most important among these are chronic rheumatism or rheumatoid arthritis the various organic diseases of the nervous system gastro-intestinal disorders and pulmonary emphysema

The frequency of various disabling illnesses in the aged can be gleaned from an analysis that was made of more than 500 000 patients discharged from hospitals in New York City in 1933 Table 1 taken from this work lists the frequency of the chief diseases encountered among hospital patients and their rate of incidence in different age groups of the population Among patients 65 years of age and over cardiovascular

diseases have by far the highest incidence Then follow malig nant neoplasms cerebral arteriosclerosis and hemorrhage fractures and cataract Diabetes bronchopneumonia and arthritis are common and have a rate of incidence higher than in the younger age groups

Most of the diseases of the aging organism that we have enumerated are popularly considered and termed degenera

TABLE 1 —FREQUENCY OF DISEASE BASED ON 487 896 HOSPITAL DISCHARGES IN NEW YORK CITY (1933)

(Rate per 100 000 population of specified age group)

D EA E	Ag		
	65 a d e	45–64	35–44
Heart diseases	2 535	1 031	337
Vascular diseases	2 110	526	96
Malignant neoplasms	1 049	531	162
Cerebral arteriosclerosis hemorrhage	798	228	30
Fractures	733	404	63
Cataract	724	169	17
Diabetes	563	317	72
Bronchopneumonia	407	144	70
Nonmalignant neoplasms	269	367	487
Arthritis	275	178	97
Tuberculosis	211	298	66
Lobar pneumonia	187	141	114
Acute appendicitis	72	109	153

W lf C l of New Y k C ty *H sp t l D ha ge St dy* (New Y k C ty 194)

tive diseases This implies that they are due to the gradual wearing out of the several tissues and organs of the body that the disease is in essence evidence of aging that it is an inevitable process of senescence Were this so we would have to accept the invalidism of aging as part of our inesca pable heritage and consider medicine as powerless to halt its progress or to restore the worn out dying organism Although the past century has witnessed a tremendous extension of the average span of life death is inevitable and we cannot ex pect an indefinite prolongation of the life span of the human

race The average expectation of life at birth for white females in the United States is 68 9 years Application of present knowledge of medicine and hygiene should make it possible to extend the average length of life to about 75 years Future medical discoveries may extend this by many years

The distinction between aging and disease is not a purely academic one If for instance we regard arteriosclerosis solely as a phenomenon of aging a process that inevitably makes its appearance in the aging arteries of every person we may well throw up our hands in the conviction that treatment is futile research fruitless If we regard arteriosclerosis as a disease process that manifests itself with particular frequency in older persons we will strive to discover its causes and marshal in its therapy all the knowledge and methods that we have at our disposal As we shall try to show in the chapter on cardiovascular diseases there is much evidence to prove that arteriosclerosis as encountered as a cause of disease among our patients is not a simple senescent process but a pathological one that may eventually be brought under control So it is with many of the other disabilities of the aged

It is important to reach a common understanding of the nature of the aging process Most people think of aging as a *terminal event as a running down or wearing out of the organism* as a final tissue and organ deterioration preceding death This is an incorrect concept Aging is but a part of the whole cycle of life Growth differentiation, involution are but different *phases of the life curve manifesting them* selves at different rates in different structures of the body The milk teeth become loosened and are cast off in child hood the thymus gland atrophies in early life the ductus arteriosus closes shortly after birth Yet these phenomena result from processes no different from those that cause simi lar organ changes in the aged As a matter of fact life

processes and organ alterations proceed at a far more rapid pace in the young than in the old Minot has pointed out that during old age the tissue and organ changes reflecting the bodily changes accompanying the time curve of life are at their slowest All of the phenomena of aging do not appear simultaneously In the same individual graying of the hair far sightedness loss of elasticity of the skin or of the arteries and decalcification of the bones occur at different ages and among different individuals there is the greatest variation in the time of occurrence of these so called stigmata of aging When we speak of senescence and aging of the organism we arbitrarily segregate the anatomical and physiological phenomena observed in older individuals and assign to them attributes of degeneration of the organism due to aging

Aging and death may result from wear and tear of the organism due to external insults from the accumulation of inhibiting substances within the organism or from a diminution or gradual extinction of the original vital force Warthin has claimed that old age may be due to gradual weakening of the energy charge set in action at the moment of fertilization of the egg It has been said that the tempo of aging is dependent less on the degree of wear and tear than on the inborn strength of resistance to this wear and tear Senescence is but one phase of the continuous development growth and differentiation of the living organism between the events of fertilization of the egg and death

It has been shown experimentally that each organ and tissue has its own time curve of aging and that this time curve depends on three factors heredity the external environment and the internal environment of the body The most important of these three elements is heredity Strains of mice can be inbred so that aging occurs uniformly in all

individuals of that strain Furthermore, it has been shown that comparing different strains of mice the anatomical changes occurring in the several organs are strain characteristics in their time of occurrence, that is that various organs age at different rates in different strains of mice We see the same phenomenon in man Longevity is primarily a family characteristic As Oliver Wendell Holmes said If you are setting out to achieve three score years and twenty the first thing to be done is some years before birth to advertise for a couple of parents both belonging to long lived families We observe as family traits early graying of the hair or early hypertension or coronary artery sclerosis Aging is primarily a constitutional phenomenon hereditarily determined It has often been suggested that hormones particularly the sex hormones may control the aging process Many have claimed that the menopause marks the first sign of aging in women and that there is a similar climacteric in men Both clinical and experimental studies give no support to this view Experimental studies have shown that the several internal secretory glands may accelerate or retard the time curves of involution of various organs but that primarily the effects depend on inherited characteristics There is no master hormone controlling senescence

The variability of the time of occurrence of the individual phenomena of growth and senescence increases greatly with the progress of the years Thus the variability of the age at which the fontanelle closes is relatively small measured in months the variability of the age at which the first teeth erupt is greater at which the permanent teeth appear still greater and at which menstruation begins still more marked The age at which presbyopia first becomes manifest shows a much greater spread So it may be expected that physical disablement due to aging will appear at widely scattered

ages say at 50 in some at age 80 in others This adds to the difficulty in determining what phenomena are due to disease and what to aging

All structural changes found in the aged are not signs of senescence The older the person the greater his years of exposure to external insults and the greater the possibility that his body will show scars of these encounters A generation ago when tuberculosis was far more widespread than it is today almost every adult at autopsy gave evidence by the scarring of his lungs that he had undergone a tuberculous infection These scars were not manifestations of aging but aged individuals because of years of exposure to tuberculous infection almost universally had been infected at some time

Often it is difficult to distinguish between phenomena of pure senescence and those of superimposed disease—a disease process whose development may be favored by the aging of the tissues Fractures of the hip through the neck of the femur are common in old persons The bone has become rarefied and brittle the aged person has lost some of his resiliency balance and coordination so that he falls more easily and the weakened bone breaks more readily Although aging plays its part the actual fracture is an accident it does not connote aging Similar considerations apply to the so called hypostatic pneumonias of the aged Loss of elasticity of the lungs rigidity of the thoracic cage diminished excursion of the diaphragm all presumably favor the collection of secretion in the lungs and prevent the expulsion of this material when the lung becomes infected The element of infection however is an accident not a manifestation of aging

The human changes most characteristic of aging bodily changes that are accepted in the popular mind too as evidence of senescence are loss in height loss in weight loss of sexual activity presbyopia deafness for high tones graying

of the hair loss of elasticity of the skin None of these alterations of the structure and texture of the body are regarded as disease processes none of them challenge the continuance of life

It has repeatedly been pointed out that natural death death from natural decay or from true senility occurs rarely in man Autopsies on old people always reveal a pathological cause of death though no symptoms were observable during life The most common causes of death in persons over 65 years of age are arteriosclerosis of the coronary cerebral or peripheral arteries hypertension carcinoma of the gastro intestinal tract prostatic hypertrophy tuberculosis and street accidents

Some practical considerations can be derived from a contemplation of these facts In dealing with older patients we should always be on the alert to distinguish between disease and aging We should not carelessly ascribe their symptoms and disabilities to the running down of their bodies At the same time we should become fully aware of the physical and mental changes that take place in the aging organism and learn how involutional alterations in the structure and function of the body may affect and alter the manifestations of disease The physician diagnoses disease as it appears in the human body he is concerned largely with the reaction of the body to disease He treats not a disease but a sick person

Disability and illness no matter at what age they occur whether in infancy or in the ninth decade should be regarded as results of disease a challenge to the diagnostic and therapeutic art of medicine Only with such an attitude can knowledge advance only with such an approach can we hope to control and prevent many of the chronic diseases of advancing years that are as yet incompletely understood

This point of view is of particular importance because of

the changing complexion of disease that has come with the aging population With the chronic diseases the chief health hazard the old methods of disease prevention through the agency of public health officials are becoming less useful The control of diabetes heart diseases or chronic rheumatism depends on an alert medical profession trained to early diagnosis and appropriate methods of treatment a public educated to be on the lookout for early symptoms and the establishment of adequate facilities for diagnosis and treatment The attempt must be made to keep well each aging individual The practicing physician will become the chief agent of preventive medicine in the field of chronic diseases

Public health officials have been slow to learn this lesson The origin of the modern preventive medicine program may be found in the reaction of social reformers to the intolerable living and sanitary conditions that accompanied the Industrial Revolution They were concerned with improving the living and working conditions of the laboring class They emphasized factory inspection child labor working hours wages housing water supplies sewage and garbage disposal With the coming of the bacteriological era physicians and bacteriologists replaced the social reformers as leaders of the public health movement and as public health officials Dazzled by the vision of eradicating disease by controlling its causative agents public health work took a totally new direction It concerned itself with water supplies with sewage disposal and sanitation with mosquito control with destruction of rats with delousing with antitoxins and vaccines The milieu in which the sick person lived became of secondary importance All of these methods of control lent themselves to mass methods of attack—improvement of water supply pasteurization of milk even vaccination

In the past decades recognition that certain infectious dis

eases do not lend themselves to such mass attack has led in the case of certain diseases to a more direct concern with the individual sick person Witness of this is the tuberculosis program with the search for early cases and contact infection and the provision of sanatorium and clinic treatment by health departments the syphilis program with the public treatment of syphilitics and the search for sources of infection by health department clinics and finally the free dispensing of serum and chemotherapeutic drugs for the treatment of pneumonia To implement their incursions into the field of the individual sick health officers have had recourse to the practice of health education of physicians and the laity With the infectious diseases coming more and more under control and with the chronic diseases becoming the outstanding health hazard the attention of public health officials is being directed along new channels Here the old methods of public health control are no longer useful The health officer approaches the cancer problem and finds he must first educate the doctor in the early diagnosis and in methods of treatment he must warn the public to be on the lookout for early symptoms he must establish cancer clinics as well as cancer hospitals equipped for radiotherapy and surgery When the health officer attempts to control other chronic diseases he must develop similar technics Although most public health officers still reluctantly enter the field of adult hygiene and chronic disease and most practicing physicians resent their incursions as an unwarranted intrusion into the private practice of medicine the bars between preventive medicine and the practice of medicine are being let down

While medicine is thus attacking citadels of disease that have heretofore been deemed impregnable and treating conditions that have in the past been regarded as the heralds of inevitable death there are some among us who are advocating

in certain cases a policy that is the very negation of orientation of medicine I refer to euthanasia—the ing of persons suffering acutely from some suppos less malady Such a procedure is a complete neg that the physician stands for and can lead only t sion from the new paths on which medicine is set

The concept of the sacredness of human life has developed through the ages and has become a dist characteristic of modern civilization At first re privileged classes it slowly was extended to ir larger groups of the population until today it has application To most it has become an articl Whether or not we accept the sacredness of hur an ethical principle we recognize a continuous tre thinking a real evolution of ideas that has gi significance to this concept in every successive o spite wars famines mass murders by autocratic g the belief that every individual life is sacred that preserved has become a basis for much of our s ization and government

If we accept this view as we must historicall be no discussion of the value of preserving or d individual life Life as such is an end in itself be voluntarily sacrificed, not to ease suffering b a more universal ideal Self preservation is ro concern of the individual it has become the re of society

Society entrusts to physicians the preservation profession of medicine is consecrated to this end cian cannot question the relative values of the treating else his hand will falter his art will s therapeutic success follows a desperate strug may be lost by a moment of doubt by a transi

of effort The true physician and successful healer must accept the sacredness of every individual life as a primary article of faith

Doubts will inevitably arise during the practice of his calling particularly among the aged A man has become mentally disorganized an affliction to himself and to his family In spite of years of effort he cannot make the needed adjustments yet he has sufficient insight into the hopelessness of his life to ask Would it not be better if I did away with myself? Another is tormented with severe physical suffering to which there seems to be no end A man awaiting execution in the electric chair develops appendicitis and needs an emergency operation to make him whole again that he may be killed Another is a brute or a criminal Then there are the hordes of congenital imbeciles of the hopelessly insane who have become institutional wards of society Some modern states in which the state is the all in all the individual nothing but a servant of the state have already proceeded to liquidate many such useless members of society The physician must brush aside all doubts all rationalization, and rededicate himself to his underlying faith to his calling as a preserver of human life

Chapter Two

THE AGING PROCESS

WE HAVE defended the view that disease in the aged is not part of the aging process that it represents a pathological condition—a challenge to diagnosis and treatment There is of course an aging process which should be recognized The clinical manifestations of disease are the results of the reaction of the body to external and internal traumas and the reaction of the aging organism differs from that of the youthful one We should endeavor to obtain a clear picture of the physical and psychological changes that characterize this aging organism because we must deal with it as the setting within which disease runs its course We must learn the range of what may be called normality for each age period and must search for means by which the slowly aging body may be made to resist the inroads of disease and premature decay

With increasing age of the organism there is a progressive dehydration of the tissues with a reduction of intracellular fluid the colloidal systems undergo alterations elastic tissue loses its elasticity Some of the outward manifestations of the underlying chemical changes in the body contribute to the characteristic stigmata of aging Chief among these are loss of weight and of stature The back becomes bowed with a gentle kyphosis The skin atrophies and becomes thinned the subcutaneous fat disappears there is loss of elastic tissue

and the skin becomes dry and wrinkled There is atrophy of the hair and sweat follicles The hair turns gray and falls out The teeth become loosened and are gradually lost

Changes in the eyes are characteristic Diminution of orbital fat leads to enophthalmos loss of tone in the muscles and skin causes drooping of the eyelids, both features combined contributing greatly to the facies of aged persons Arcus senilis although not confined to the aged is common in elderly individuals Finally presbyopia loss of accommodation is one of the most definite evidences of aging Careful statistical study has shown a genuine correlation between the age of onset of presbyopia and length of life

Impairment of hearing particularly for high tones begins at about age 50 and slowly progresses It is due to simple atrophy of the nerve and the end organ in the cochlea and is an almost universal accompaniment of aging

Parallel with these signs that are discernible by the layman and that together constitute the picture of the aged person there are analogous changes in the internal organs These will be discussed in the chapters devoted to the several organ systems In their totality these changes of the organism lead to changes in function When he is at rest or under no great physical strain the bodily functions of the aged person are adequate for his needs The fasting blood sugar level tends to be slightly higher in the old than in the young This may be due in part to an increased renal threshold of sugar excretion Sugar tolerance tests in persons over 65 commonly reveal an excessive rise of the blood sugar level and delay in its recession to the previous level [1] Both the urea clearance and the concentrating power of the kidneys decline with age and there is a slight elevation of the blood urea

[1] Marshall F W "The Sugar Content of the Blood in Elderly People" Quart. J Med 24 257 1931

nitrogen There is said to be an increase in the blood choles terol[3] A progressive decrease in the total and vital capac ities of the lungs and an increase in the residual air become manifest particularly after the age of 60 These result from alterations in the thorax and spine that limit the mobility of the thoracic cage as well as from loss of elasticity of the lungs[4] Calcification of the costal cartilages begins in the second decade of life becomes accelerated at age 20 and continues more slowly after age 40 By the sixth decade the first costal cartilage is about 80 per cent calcified Full cal cification occurs about 10 years later in women than in males in Negroes the process begins earlier in life and reaches its maximum at an earlier age[5] The temperature of the body the cardiac output the respiratory exchange compare favor ably to similar functions in youth

As soon as the aging body is exposed to unusual or greater strain we find that the range of response of the various organs is curtailed and that the power of self regulation of the body to maintain a constant internal environment the function that Cannon calls homeostasis is lost An aged per son does not tolerate excessive cold or heat he cannot adapt himself to extreme environments His heart functions well when little demand is made upon it but it cannot respond to the load of greater exertion So it is with all of the bodily functions With age the bodily reserves are encroached on more and more and gradually these physical limitations circumscribe the range of response and capabilities of the

[2] Lewis W H Jr and Alving A S "Changes with Age in the Renal Function of Adult Men" Am J Physiol 123 500 1938

[3] Rafsky H A and Newman B Cholesterol Studies in the Aged" J Lab & Clin Med 27 1563 1942

[4] Kaltreider N L *et al* The Effect of Age on the Total Pulmonary Capacity and Its Subdivisions Am Rev Tuberc 37 662 1938

[5] Michelson N The Calcification of the First Costal Cartilage Among Whites and Negroes Human Biol 6 543 1934

organism Whereas the young person can abuse his body and overtax his strength with few deleterious results such efforts in the aged soon lead to disaster

The process of repair of tissues after injury is altered in the aging organism It has been shown experimentally that in senescent animals the power of instituting normal repair for epithelium in certain organs is modified or lost Du Nouy has demonstrated that wounds cicatrize much more slowly in older than in younger individuals This has direct bearing on the problem of operations in the elderly

With progressing age there is a gradual change in the natural resistance of the body to infection This may be attributed in part to atrophy of the glands of internal secretion of the spleen the macrophage system the bone marrow and the lymphatic tissue structures that are concerned with immune processes Nutritional deficiencies which are so common in the aged particularly inadequacy of certain vitamin stores and of calcium lessen the organism s power to resist infection Pathological changes in various organs that become increasingly frequent with advancing years bring about a lessened local or organ resistance to infection Thus pulmonary emphysema favors the development of bronchitis and bronchopneumonia prostatic enlargement or large cystoceles allow of ready infection of the bladder circulatory impairment in the extremities often leads to serious infection and gangrene Types of infection vary in young and old This may be due in part to an acquired immunity to many diseases and to different chances of exposure to the several infecting agents Rheumatic fever and typhoid fever are rarely encountered among the aged Pulmonary tuberculosis is common but manifests itself usually as an indolent fibroid phthisis that is often misdiagnosed as chronic bronchitis On the other hand pyogenic infections bronchopneumonia and

erysipelas occur with increased frequency among the aged Erysipelas occurs more commonly in the decade 60 to 70 than in any other if morbidity is estimated by age specific rates

The death rate increases 8 per cent each year throughout life following a logarithmic equation Statistical analysis shows that this effect of age on death rate is due not to the accidental accumulation of infections or injuries but to the loss of resistance to disease as a result of an underlying aging process If accumulated injuries were the cause of senile mortality we should encounter occasional individuals living to exceptional ages such as 150 years The increased death rate as such is a manifestation of aging[6]

With age there is a slow decrement in all of the functions and in the psychological reactions of the body There is impairment of bodily strength and of swiftness and exactness of motion But there is great variability in the time of appearance of these changes, and many a superior oldster may in these functions excel the average younger individual There is a general belief that old persons have lost the faculty of learning new disciplines and new procedures that they are resistant to new ideas Psychological studies have thrown doubt on this view and many believe that the educability of a person does not necessarily decline with age The liberalism or conservatism of his outlook on life is a determinant as important as his chronological age Certainly wisdom a function involving experience and judgment is preserved in age

Impairment of memory is universally accepted as a stigma of aging Memory is a function of attention The physical weakness of the aged and the assumption by society that they are no longer useful lead to a sense of inadequacy and to a withdrawal of attention Lack of memory thus is often actu

[6] Simms H S "The Problem of Aging and of Vascular Diseases" Science 95 183 Feb 20 1942

ally lack of attention Older people are more conservative than the young they resist changes in their mode of life, they resist new ideas in manners and morals Again this is not necessarily the result of senile changes in their brains and modes of thought but may result from the sense of inadequacy which their insecure position in society impresses on them which gives them an emotional need for an unchanged world

Many of the mental and emotional changes manifested in elderly persons are due less to aging and regression of their mental faculties than to the kind of life forced on them by a heedless society Lawton has pointed out that economic and social insecurity plays a large part in hastening mental deterioration in older persons A man who has worked most of his life who has supported and brought up a family who has regarded himself if he ever gave thought to the matter as a useful member of society is suddenly without work and without income for reasons of age alone In spite of his best efforts current concepts and customs make it impossible for him to obtain employment and maintain his independence He becomes dependent on his children or on society He learns that he has no further function in life yet instinctively he clings to life This change in his status forced on him by the workings of the culture of the society within which he lives rather than by any cause residing within himself colors his mental and emotional reactions We draw the unwarranted conclusion that many of the mental and emotional characteristics of the aged are caused by intrinsic biological changes instead of recognizing that they are the result of external conditions imposed on them by the cultural pattern of the society within which they live The validity of this view is strengthened by the repeated observation of intellectual vigor and emotional balance in individuals who have passed the eighth decade of life and who because of certain

fortunate circumstances can continue lives of financial independence and intellectual or creative productivity

An old person who is living a vigorous, useful life regards with resentment the physical disabilities that gradually overtake him He is annoyed and disturbed that he must now give some heed to his much abused body The old man who is living an aimless life is much more apt to cultivate his disabilities and to learn to live for them alone In treating his aging patients the physician should give due regard to these social and psychological problems that so largely determine the patient s reaction to illness and disability To retard the process of mental senility he should address himself not alone to the task of controlling the progress of organic disease but of maintaining his patient as a useful member of society The second part of this undertaking is often far more difficult than the first and will lead the physician beyond the rigid domain of medicine

A new concept of aging and disease was advanced by the Russian scientist Bogomolets[7] If confirmed it may have a far reaching influence on our views of senescence and on the treatment of many chronic diseases Bogomolets conceived of the connective tissues as a physiological system whose functions are basic to the activities of all organs and to all other processes in the body It has a *trophic* function regulating cellular nutrition and metabolism a *plastic* function that is concerned with the healing of wounds and the regeneration of tissues a *protective* function related to phagocytosis and the tissue reaction to new growths an *autoregulative* function resulting in the formation of stimulating substances especially by the spleen and a *mechanical* function as an osseous and elastic skeleton Bogomolets believed that the

[7] Bogomolets A A Antireticular Cytotoxic Serum as a Means of Pathogenetic Therapy" Am Rev Sov Med 1 101 1943

physiologic age and the health of the body are determined by the condition of the connective tissues and that the physiologic state of the connective tissues affects all kinds of diseases as well as the process of aging

He developed an antireticular cytotoxic serum which is prepared by injecting into a horse, cells of the spleen and bone marrow of a healthy person who has died suddenly Large doses of this serum injure the connective tissues but small stimulating doses are said to stimulate the plastic, protective and trophic functions of the connective tissues and so assist the natural healing power of the body This serum has had widespread use in Russia, and Bogomolets and his colleagues reported remarkable results in modifying the course of various infections, in preventing recurrences after operative removal of cancers and in accelerating the healing of fractures and of wounds Bogomolets further suggested that the serum might by prolonging the physiologic activity of the trophic functions of the connective tissue, furnish a means of postponing senescent changes in the body

Chapter Three

GENERAL MANAGEMENT OF THE AGING AND AGED PERSON

THERE IS no short cut to the maintenance of health and the prevention of disease in the aging The diseases to which the aging person is subject are insidious in onset and chronic in course Their causes are in large measure unknown Methods for the prevention of disease must be directed along the channels of individual hygiene and periodic examinations designed to discover abnormalities of function and structure at their first appearance and in their earliest stages To achieve this end the stereotyped periodic health examination performed in a routine manner is insufficient It is necessary to include a survey of the daily life of the patient his habits his mental and psychological make up and his relationship to his wife his children his business and his environment The physical examination should lay special emphasis on the discovery of defects which are known to occur in the aging organism The physician should always keep in the forefront of his mind that it is his primary function to preserve the aging person as a useful member of society with a normal relationship to the world about him In his enthusiasm to treat specific abnormalities the physician is apt to overlook the fact that a too drastic change in the patients mode of

life may have unfavorable psychological consequences that far outweigh the benefit that may be derived from the proposed regimen When specific medical measures are life saving there is no choice When the issue is one of balancing the value of retirement from work and dedication of the patient s whole life to the preservation of his health against some compromise plan by means of which the patient may still feel that his term of usefulness is not yet ended the physician should always endeavor to work out a plan that will preserve the patient s individuality and self respect Far too often doctors recommend complete retirement uproot the patient from the community where he has spent all of his life and send him to a place like Florida or California No generalization can be made in these matters but in every case the physician should keep in mind that he is treating a person and not a disease In the treatment of acute diseases such as pneumonia or acute surgical conditions this factor is of relative unimportance but in the adjustment of a patient s life in the endeavor to retard the progress of a chronic illness social and psychological factors loom large Indeed it is probable that a suddenly enforced retirement the resulting idleness and sense of uselessness the overwhelming realization that the life one has lived and striven for is finished may hasten the progress of disease and even favor early death It is probably more than a coincidence that one reads so frequently of the sudden death of a sea captain for instance a few months after his retirement from active service

Of course a time comes when every man or woman should be relieved of the heavy routine of maintaining himself in competition with the younger generations that tend to crowd him out The tasks of the aging should be lightened This process can be gradual The patient can substitute certain new interests for the old he can preserve some sphere of usefulness a grandmother can carry on some household duties

or the old man can still do light chores on the farm or similar tasks in the home Thus the transition can be made without the shock that a complete scrapping or a discarding of the aging individual inevitably brings about

In treating aging persons the physician should give constant consideration to the loss of youthful resiliency and adaptability of their tissues and organs and to their progressively lessened range of response to the calls made on them by the demands of daily living The young person can abuse his body almost with impunity he can exercise to complete fatigue he can permit himself excesses in eating and drinking he can smoke too much he can go without sleep His recuperative powers are great and rarely does he do himself permanent damage But when middle age is passed the body can no longer adapt itself so readily to extreme stresses soon some structure or function gives way and leads to the beginning of disease Thus with advancing years the individual must learn to know his increasing limitations and arrange his living so that he does not overtax the weakening organism Here again one should try to strike the balance between the maintenance of physical fitness and excesses that lead to overstrain

Nutrition

There exists a balance between the food requirements of the body and its rate of growth and degree of activity Food requirements are in reality energy requirements for food provides the source of growth and energy Thus changing expenditures of energy are paralleled by change in the quantity of food needed The caloric needs of the growing child per kilogram are far greater than those of the adult of the laborer greater than of the sedentary clerk Most of us as we pass middle life involuntarily manifest a slowing down and diminution of our physical and sexual activities But

appetite and food consumption are largely matters of habit they are not automatically adjusted to the actual caloric needs of the body So it commonly happens that after the age of 40 food intake is in excess of the energy requirements of the body and adiposity results Increase in adipose tissue and the development of the panniculus adiposus with the resultant pot belly are almost universal in middle age It is only when the seventh decade is passed that a loss of weight occurs, due in large measure to loss in water content of the tissues

With increasing age there is a gradual lowering of the basal metabolic rate At the age of 60 the reduction is about 10 per cent and in extreme senescence it may reach 25 per cent This lessened oxygen consumption is caused in part by involution of the thyroid gland in some measure by diminution in muscular vigor It contributes to the lessened food requirements of the aging body

The caloric needs of a man living a quiet life indoors are about 2 200 calories of one engaged in a sedentary occupation 2 500 calories and of one leading a more active life 3 000 calories A worker at heavy tasks such as carpentry, needs about 4 000 calories and one engaged in exceedingly laborious work such as lumbering 6 000 calories It is evident that with advancing years and lessened physical activity the caloric needs diminish Absolute figures cannot be set down for each age group but the principle is clear that as a person grows older his food intake should be cut down Most persons past 70 who live very quiet lives should consume between 1 500 and 1 800 calories daily

The protein needs of the average adult are placed at about 75 Gm a day The aging body needs less protein and is less able to handle an excess of ingested protein The protein intake should be reduced in proportion to the reduction in caloric intake Thus an old man whose requirements are

TABLE 2.—Weight-Height-Age Tables (in Ordinary Street Costume)

Men

Age		5 1	5 2	5 3	5 4	5 5	5 6	5 7	5 8	5 9	5 10	5 11	6	6 1	6	6 3	6 4	6 5	Age
40	131	133	135	138	141	145	149	153	158	163	168	174	180	180	193	200	00	-1	40
41	131	133	135	138	141	145	149	153	158	163	168	1 4	180	18	193	00	-07	-13	41
42	132	134	136	133	14	146	150	154	159	164	165	175	181	187	194	01	08	214	42
43	13	134	136	139	14	14	150	154	1 9	164	169	1 5	181	187	194	-01	08	14	43
44	133	135	137	140	143	147	151	155	160	165	170	1 6	1	188	195	0	09	215	44
45	133	135	137	140	143	147	151	155	160	165	1 0	1 6	182	188	195	07	-09	215	45
46	134	136	138	141	144	148	15	1 6	161	166	171	177	183	189	196	03	210	16	46
47	134	136	138	141	144	148	15	156	161	166	171	1 7	183	190	197	04	11	17	47
48	134	136	138	141	144	148	152	156	161	166	171	1 7	183	190	197	04	11	17	48
49	134	136	138	141	141	148	15	156	161	166	171	177	183	190	197	04	11	-17	49
50	134	136	138	141	144	148	152	156	161	166	171	1	183	190	197	04	211	217	50
51	135	137	139	14	145	149	153	157	162	167	17	1 8	184	191	198	20	21	218	51
52	135	137	139	142	145	149	153	157	163	167	17	178	184	191	198	-05	1	218	52
53	135	137	139	142	145	149	1 3	157	16	167	17	178	184	191	198	0	1	218	53
54	135	137	139	14	145	149	153	158	163	168	1 3	1 8	184	191	198	05	21	219	54
55	135	137	139	14	14	149	1 3	158	163	168	173	178	184	191	198	05	-1	-19	55

Women

Age	4 8	4 0	4 10	4 11	5	5 1	5	5 3	5 4	5 5	5 6	5 7	5 8	5 9	5 10	11	6		Age
40	119	121	123	1 5	127	129	13	135	138	14	146	1 0	154	158	161	164	167		40
41	1 0	1	1 4	1 6	1 8	130	133	136	139	143	147	151	1 5	1 9	16	165	168		41
4	1 0	1	1 4	1 6	1 8	130	133	136	139	143	147	151	155	159	16	166	169		4
43	1 1	1 3	1 5	1 7	129	131	134	137	140	144	148	152	1 6	160	163	167	170		43
44	1	1 4	1 6	1 8	130	13	135	138	141	145	149	153	157	161	164	168	171		44
45	1 2	1 4	1 6	128	130	132	135	138	141	145	149	153	157	161	164	169	171		45
46	123	1 5	1 7	1 9	131	133	136	139	14	146	150	154	158	162	165	169	17		46
47	123	1 5	127	1 9	131	133	136	139	142	146	151	155	1 9	163	166	1 0	1 3		47
48	124	1 6	1 8	130	133	134	137	140	143	147	1	1 6	160	164	167	171	1 4		48
49	124	1 6	1 8	130	13	134	137	140	143	147	15	156	161	165	168	1 2	175		49
50	1 5	127	1 9	131	133	135	138	141	144	148	1 2	156	161	165	169	173	1 6		50
51	125	1 7	1 9	131	133	135	138	141	144	148	152	157	162	166	170	174	177		51
52	125	127	1 9	131	133	135	138	141	144	148	152	157	162	168	170	174	177		5
53	1 5	1 7	1 9	131	133	135	138	141	144	148	152	157	162	166	1 0	174	177		53
54	1 5	127	129	131	133	135	138	141	144	148	153	158	163	167	171	174	177		54
5	1 5	1 7	129	131	133	135	138	141	144	148	153	1 8	163	167	171	174	1 7		55

filled by 1 500 calories a day should reduce his protein intake to about 45 Gm

Weight Reduction

The maintenance of an optimum weight in his patients is one of the primary concerns of the physician particularly in those past middle age Life insurance tables have demonstrated that after age 35 overweight is associated with a high death rate and that after 45 overweight is a serious health hazard. Table 2 presents the optimum weight for men and women and can be used as a rough guide Such figures cannot be used arbitrarily for some persons have heavier bones and bodily frames than others so that their normal weights are greater than those of the average

In most instances satisfactory weight reduction can be achieved without adherence to a rigid written diet It is much better to explain to the patient the principles of nutrition that he is to follow and to work out with him the modification of his diet that will achieve the desired end It is astonishing how relatively small dietary adjustments may bring about a sufficient loss in weight. The first step is to reduce the intake of carbohydrates bread potatoes rice noodles cake and pastry and the like Often this is all that is necessary In other cases reduction in the size of the portions is effective The patient is instructed to leave the table a bit hungry rather than uncomfortably full. Eating between meals taking soft drinks ice cream candies or a snack before retiring add greatly to the caloric intake Alcohol has high fuel value and a few cocktails or high balls may add several hundred calories to the daily consumption. Beer too is of high caloric value Bacon and other fatty foods foods prepared with olive oil or butter mayonnaise large helpings of butter can be

easily eliminated Most patients can lose weight satisfactorily by such an adaptation of their diet planned with understanding in cooperation with their physician It is unnecessary to attempt to induce a rapid drastic reduction in weight It is better for the patient to lose from 1 to 2 lb a week consistently and in the meantime become habituated to his new

TABLE 3 —1,200 CALORIE DIET

BREAKFAST	
Fruit	1 serving
Bacon	1 slice crisp
Egg	1
Bread	½ thin slice
Butter	1 square
Cream	1 tablespoon
Coffee or tea	
LUNCHEON	
Meat	1 large serving
Vegetable	2 small servings
Butter	½ square
Fruit	1 serving
Milk (skimmed)	1 glass
DINNER	
Meat	1 large serving
Vegetable	1 small serving
Salad vegetable	1 small serving
Butter	½ square
Fruit	1 serving
Milk (skimmed)	1 glass

dietary plan Such a procedure is much more apt to lead to permanent nutritive balance To a large extent habit governs the nature and quantity of food consumed For the first few weeks the patient may complain of hunger but he soon becomes accustomed to the new regime and can continue it with perfect comfort

There are some who do not respond to such simple measures Some patients cannot be made to realize the importance of an adjustment of their dietary habits Such persons

must be given the bald facts of the increasing mortality that accompanies overweight and the whole situation must be dramatized for them In these cases it is wiser to prescribe a formal written dietary The patient may be maintained on a 1 200 calorie diet until the desired weight reduction is achieved Then certain increases may be allowed in order to maintain the ideal weight There are patients who do not lose weight in spite of rigid adherence to a limited diet Often this refractoriness is due to water retention This is favored by excessive ingestion of salt or of sodium bicarbonate The retained water can be driven off through the kidneys by occasional intravenous or intramuscular injection of a mercurial diuretic such as mercupurin or salyrgan The patient diets strictly for about a week and is then given a 2 cc injection of the mercurial diuretic Usually a 3 to 5 lb weight loss will follow diuresis and this weight loss will be maintained The diet is continued and every week or two another injection is given until the desired result is achieved Before giving such mercurial diuretics the physician should make sure that there is no serious kidney disease that may be aggravated by the mercury A trace of albumin or a rare cast is no contraindication but in the presence of true renal impairment signalized by low specific gravity of the urine the drug is best avoided

Obesity is rarely caused by endrocrine disorders [1] and the administration of thyroid is usually unnecessary When the measures already outlined do not succeed it is well to determine the basal metabolic rate of the patient Readings ranging from minus 10 to minus 20 do not indicate a true thyroid deficiency unless there is an accompanying elevation of the blood cholesterol However in such cases the administration of desiccated thyroid may be helpful It should be given cautiously with the patient under regular observation It is

[1] Newburgh L. H and Conn J W Obesity " Physiol Rev 24 18 1944

well to begin with 1 gr of desiccated thyroid daily and to increase the dosage gradually to a maximum of 3 gr if no weight reduction is obtained Symptoms of thyroid intoxication are an increase in pulse rate increasing nervousness, palpitation and sleeplessness If such symptoms supervene the drug should be discontinued

Even in the old obesity may be conditioned by a psychoneurosis Many people claim that unless they eat at frequent intervals they feel weak and are overcome by fatigue They are miserable unless they are constantly eating Actually this is a mechanism that momentarily assuages the anxiety or relieves the loneliness that evokes the feeling of weakness Weight reduction may be unsuccessful without treatment of the underlying maladjustment or psychic disturbance

Diet

Diet is not all a matter of calories and the maintenance of an ideal weight Experimental studies in nutrition have demonstrated an intimate relationship between the qualitative composition of the diet and health They have shown that inadequate diets may cause disease and that the duration of life of individual animals and the health of successive generations can be affected at will by alterations in the diet One should distinguish between a minimum adequate diet and an optimum diet For instance rats kept on a suboptimum diet develop and grow normally but if this same diet is continued for several rat generations a gradual deterioration of the succeeding generations takes place Sherman has shown that prolongation of the period of the prime of life and an actual extension of the span of life may be brought about in rats kept on an optimum diet In his words Preservation of the characteristics of youth and extension of the prime of life

are very significantly aided by the taking of a liberal propor tion of the needed calories in the form of protective foods" McCay has demonstrated that retardation of the growth of rats by reducing the calories of an otherwise complete diet will delay and slow the onset of maturity and will greatly prolong the life span He believes that retardation of growth affords a method of retarding senescence and of extending the life span Cataracts have been produced in rats by diets high in lactose or galactose (lactose liberates galactose in the body) and low in fatty acids and protein The common oc currence of cataract in patients with diabetes another condi tion with perverted sugar metabolism is well known

Whereas these experimental data cannot be directly carried over to the field of human nutrition they yield significant leads The results of inadequate dietaries may be slowly cumulative and may not become apparent for many years Many of the manifestations of aging and disease in older persons that today are accepted as inevitable results of senes cence may well be the result of life long faulty dietaries Sherman has repeatedly emphasized that the ordinary Ameri can diet is more deficient in calcium than in any other ele ment As a result adults experience a steady long continued loss of calcium through the years This does not become superficially manifest because the great calcium stores in the bones constantly make up for the calcium losses in the blood and tissues But as a result of this constant depletion the bones become poor in calcium and more fragile Osteoporosis of the aged may be the result of a dietary fault and not an inevitable accompaniment of aging An intake of almost 1 Gm of calcium a day is needed to maintain the calcium bal ance of the body Most foods are poor in calcium The best sources of this mineral are milk which contains about 1 Gm to the quart cheese and green leafy vegetables

Snapper has pointed out that arteriosclerosis occurs rarely in northern China in spite of the fact that diabetes is common He suggests that fundamental differences in dietaries may underlie this phenomenon The Chinese diet contains only small amounts of cholesterol but considerable quantities of unsaturated fatty acids especially linoleic and linolenic acids He states that the average cholesterol content of the blood of the Chinese is lower than that of Westerners and suggests that this may account for the lessened incidence of lipoid infiltration of the arterial wall among the Chinese

As yet we have no knowledge of a specific relationship between individual vitamins and aging but in the light of the experimental work referred to in the previous paragraphs it is evident that the provision of an adequate supply of vitamins throughout life will help to maintain health and probably postpone some of the disabilities that come with advancing years We have learned to recognize the more extreme manifestations of vitamin deficiencies and have become aware that vitamin deficiency may give rise to disease under unexpected circumstances Today we know that symptoms of beriberi due to lack of thiamine hydrochloride are common in alcoholics who eat little for many weeks and derive most of their calories from alcohol We see symptoms of pellagra in persons who eat inadequately or who have serious gastrointestinal disease preventing absorption of nicotinic acid and riboflavin At times we see scurvy in patients with peptic ulcer who are kept too long on a rigid Sippy regimen Some of the mental disturbances of the aged have been shown to be pellagra like and have been cured by the administration of nicotinic acid It is not at all unreasonable to suppose that many of the lesser disturbances that develop with aging are ascribable to die

[2] Snapper I *Chinese Lessons to Western Medicine* (New York City Interscience Publishers Inc 1941) p 160

tary deficiencies Often a primary disease such as a heart disease will interfere with the appetite and with the absorption of food so that secondary symptoms due to dietary deficiencies become manifest In older persons we may encounter dietary fads and idiosyncrasies that lead to disease

Thus in planning the diets of the middle aged and elderly we should concern ourselves not with calories alone but with the composition of the diet to insure an adequate representation of foodstuffs containing the protective vitamins and the needed minerals Vitamin A is found particularly in milk butter eggs cheese liver and the green leafy vegetables vitamin B in whole wheat bread beef mutton and many fruits and vegetables vitamin B in milk fruits and the leafy vegetables vitamin C in fruits especially oranges limes lemons tomatoes and melons

Cheilosis the macerated lesion at the angles of the mouth has been considered pathognomonic for riboflavin deficiency Recently it has been shown[3] that this lesion in older persons is often due to ill fitting artificial dentures with too short vertical dimension causing the upper lip to overhang the lower This allows the saliva to escape at the angle of the mouth and creates a moist pocket where fungi and bacteria grow on the epithelial debris The lesion is more fissured and granulomatous than that caused by ariboflavinosis It disappears when proper dentures are provided In true ariboflavinosis there are accompanying lesions of the lip

Another handicap that must be overcome in planning diets for the aged is the impairment of chewing power due to loss of teeth and to diseased teeth It is most important to see to it that every aging person has dentures that will enable him to masticate an adequate varied dietary An old person com

[3] Ellenberg M and Pollack H Pseudoariboflavinosis" J A M A 119 790 July 4 1942

monly restricts his dietary to cereals soft bread and tea and coffee because he cannot chew most of the food that is set before him

With age too there is apt to be more difficulty in digestion There is as a rule a diminution in gastric juice particularly in hydrochloric acid there may be motor disturbances of the stomach and intestines constipation and the accumulation of gases are common These in turn lead to inadequate absorption of food from the gastro intestinal tract and to dietary idiosyncrasies because of the patient s attempt to correct the gastro intestinal distress

Thus the diet of each person should be individualized with due reference to the factors that have just been discussed Its quantity should be adjusted to the correct caloric needs of the individual its composition should be sufficiently varied to provide not a minimum but a surplus of the necessary vitamins and minerals its consistency should be adapted to the masticatory power of the patient and finally it should be adjusted to the digestive peculiarities of the individual As a general rule a varied diet including fruits meats fish vegetables particularly the green leafy varieties eggs and milk should serve the purpose One of the most difficult tasks is to provide an adequate calcium intake i e almost 1 Gm a day If the patient will drink 1 qt of milk a day the problem becomes simple If he will eat liberally of the leafy green vegetables and some cheese daily the amount of milk can be reduced

In many cases it is necessary to supplement the diet with some of the vitamins The most important ones for elderly persons are vitamin A and vitamin B complex Calcium may be given as calcium lactate 15 gr three times a day or calcium gluconate 30 gr three times a day Forty grains of calcium lactate or 75 gr of calcium gluconate contain as much cal

cium as 1 pt of milk Calcium is best given on an empty stomach at least three hours after the previous meal

Diminution in the sense of taste comes with aging This may interfere with appetite and may make it difficult to persuade an older person to eat a greater variety of food He becomes satisfied with a simple monotonous diet Condiments may be allowed freely unless some specific disease condition contraindicates their use

In order to avoid overtaxing the digestive apparatus it is best to plan for three meals of almost similar size instead of making the evening meal the heaviest one Indeed it is wise to have an elderly person partake of his main meal in the middle of the day and take only a light supper It should be habitual to rest for an hour or so after each meal This aids digestion and avoids overtaxing the heart Both the digestive process and muscular activity call for an increased blood flow and the aging heart may not be competent to meet both needs simultaneously without damage to itself

Tea and coffee one or two cups daily may be freely allowed These beverages are useful mild circulatory stimulants and diuretics They rarely do harm unless there is a personal idiosyncrasy to them In some persons coffee causes digestive disturbances in others extrasystoles Coffee may cause wakefulness when taken with the evening meal

Alcohol in moderation is very useful to the aged It serves as an appetizer and in cachexia and malnutrition is helpful because of its food value Reflexly it acts as a dilator of the peripheral blood vessels and promotes a sense of warmth and well being Most valuable is its depressant action on the central nervous system Taken when the subject is worried tense or overtired it promotes relaxation and rest and may induce sleep A glass of sherry or whiskey or some wine taken in the late afternoon after a fatiguing day is very beneficial

and a drink taken before retiring may promote sleep Of course it should be taken in moderation The Regimen Sanitas of Salerno written some 800 years ago sums up the case for alcohol

> Sound wine revives in Age the heart of youth
> While poor wine acts the other way forsooth
> Pure wine on all refreshment will bestow
> In brain and stomach cause a cheerful glow
> And stagnant currents force anew to flow
> 'Twill all depressing carking gloom remove
> Sharpen the mind and also sight improve
> Quicken the ear and the whole body nourish
> And cause old age with youthful bloom to flourish

Rest and Exercise

It is difficult to strike a balance between rest and exercise in the aging individual Rest is certainly better than uncontrolled exertion but measured and regulated bodily activity has positive physical as well as psychic benefits

Although the movement of the blood finds its origin chiefly in the cardiac muscular pump the regulation of the circulation is determined by many additional structures and functions such as the vasomotor tone the distribution of blood in the arteries capillaries and veins the blood volume the respiration and the action of the voluntary muscles in milking the blood in the veins toward the heart It is common knowledge that physical training enables an individual to undergo severe bodily exertion with greater ease and efficiency A series of complex physiological adjustments makes this possible Through the development of the voluntary muscles and their increased coordination through the agency of the central nervous system movements are executed with less effort useless motions are eliminated and less oxygen is needed by

the body to accomplish an equivalent amount of work The chest expands the vital capacity becomes greater so that pulmonary ventilation is more readily increased The heart muscle like the striated muscles undergoes some hypertrophy and has greater contractile power The nervous regulation of the heart and blood vessels is more coordinated and there is a closer adaptation of cardiovascular response to the needs of the body The pulse rate in the trained individual is slower and since the minute volume flow of blood is unchanged the output per beat is greater The blood pressure is lower The oxygen carrying power of the blood may be increased and there is better oxygen utilization by the tissues All of these factors give the body a greater range of response to exercise The increase in pulse rate minute volume flow of blood and blood pressure induced by exercise is less in the trained than in the untrained

These circulatory reactions and adaptations to exercise and training apply to elderly persons as well as to young athletes While there is no thought of making a trained athlete out of a man advanced in years a moderate amount of well tolerated activity serves to make the circulatory apparatus a more efficient machine spares the heart a certain amount of work ordinarily carried by the peripheral circulation and promotes a general sense of well being It also helps to prevent obesity which follows a too sedentary life and is an added burden to the heart

These considerations lead to the conclusion that in persons past the age of 50 one should aim to maintain physical fitness without permitting too strenuous activity Sudden spurts of effort as in lifting heavy objects or sprinting to catch a train are particularly hazardous for they may induce acute heart failure Similarly all competitive sports in which the sense of rivalry makes the participant forget his fatigue and drives

him to greater efforts should be prohibited It is difficult to formulate absolute rules A man who has labored physically all his life can often continue at his occupation into his seventh decade although one encounters few such men who continue at their work with undiminished vigor after the age of 60 But in such men too it is wisest to avoid sudden severe strains as in lifting The average man who leads a more or less sedentary life had better give up the more strenuous sports such as tennis and handball particularly if he plays only occasionally There are men who continue playing tennis until they are well up in their sixties but they are exceptional A good deal depends on the intensity with which the game is played Golf is well tolerated by most aging individuals and moderate swimming too is permissible Dancing places a much greater strain on the heart than is generally recognized It is not unusual for the heart rate of normal young individuals to rise to as high as 120 to 150 beats a minute after three or four minutes of dancing Walking hiking golfing horseback riding are probably the best activities for the person past 50 The housewife too should gradually give up the more strenuous aspects of her work such as scrubbing floors and doing heavy laundry The best guide to the degree of activity that may be allowed is the reaction of the individual Undue fatigue dyspnea precordial distress are all signs that the individual is overtaxing himself Above all it is important that a man who has lived a completely sedentary life undertake new physical activities gradually and slowly try to get himself into better physical trim It may be well to repeat that it is the unexpected sudden severe physical strain that is apt to damage the aging body

Stair climbing traditionally is a great bugaboo to elderly *persons as well as to those with heart disease* Stairs are not

nearly as dangerous or harmful as we make our patients believe Persons with good cardiac reserve may climb stairs freely but unhurriedly it does them no harm Running up, two steps at a time is unwise

We should teach the middle aged and elderly person to observe unhurried free activity and with it a sense of leisure It is the everlasting rush from one place to another from one task to the next that is wearing and that causes undue strain

Climate and Weather

There is no difference in the longevity of people living in different climates so that climate alone cannot be credited with a determining influence on the aging process It is true that old people do not stand the cold well and many of them have emphysema and recurrent attacks of bronchitis that are induced and aggravated by the changeable weather of our north temperate climate For such a winter residence in the South in Florida or in California is often beneficial However only the minority can avail themselves of this resource

Temperature regulation of the body is less efficient in the aged than in young persons Elderly persons should avoid extremes of heat and exposure to the sun The mortality rates from heat stroke are 8 per 100 000 at ages 70 to 79 and 20 per 100 000 at ages 80 to 89 The aged suffer heat stroke or sunstroke more readily than do younger persons The sensitiveness of the aged to cold is well known Institutions for the aged must maintain a higher temperature in their rooms than institutions harboring younger persons A temperature of 75 F is usually gratefully experienced by an old person During the winter the environmental temperature of the aged should be maintained at a comfortable warmth For the same reason the aged should dress more warmly than younger people

When they go out their movements are slow their physiologic responses sluggish they cannot generate enough heat through muscular action to compensate for exposure to freezing temperatures So it is well for old people to wear warm woolen underwear and warm socks and to bundle up in warm garments when they venture out in frigid weather Warming the bed at night or the use of a hot water bag contributes to their health and comfort

It is unwise for men in the sixth and seventh decades of life to undertake severe physical exertion in the cold Cold reflexly may cause narrowing of the coronary arteries and this combined with heavy work may induce coronary insufficiency and cardiac infarction Every year one reads of men past the prime of life experiencing heart attacks while shoveling snow or while struggling through a blizzard I see at least half a dozen such cases annually

In bathing too the aged person should avoid extremes of hot and cold Baths that are too hot are enervating and weakening and may cause collapse Cold baths may be too great a shock to the heart and circulation and in an arteriosclerotic person may cause coronary insufficiency

Sleep

Most persons need less sleep as they grow older The normal adult usually sleeps some eight hours every night Many find their need for sleep gradually reduced after the age of 50 and may do well with six hours of sleep It is claimed that after the age of 65 many individuals sleep only four hours out of the 24 but this must be exceptional Many persons as they grow older and feebler sleep more as much as 12 hours a night The duration and character of sleep even in youth is a highly individual characteristic varying

greatly among individuals No arbitrary optimum figures can be set Each person should sleep long enough so that he awakens rested and refreshed whether this be five hours or 10 hours Whereas the younger person can voluntarily curtail his hours of sleep for a while the elderly individual cannot do so without showing signs of fatigue and inefficiency Slowness of recuperative power and lack of elasticity and adaptability of all physiological functions are the major accompaniments of aging The aging individual cannot abuse his body as can the youth without paying the penalty of increasing the inefficiency of his involuting body Many old persons spend a full eight to 10 hours relaxed in bed and are satisfied if they sleep only part of the time Others continue to go to bed at the hour to which they were accustomed when they were younger and needing less sleep, awake early and complain of insomnia Such persons are helped by postponing the hour of retirement

An afternoon nap has great restorative value and should be adopted as a routine by most aging persons A short sleep 15 to 30 minutes is better than a long one With prolonged sleep there comes such complete muscular relaxation that awakening is difficult and the individual often feels more tired than before he fell asleep After the age of 70 especially in persons with progressive enfeeblement the need increases for short naps throughout the day Such persons often fall asleep while sitting in a chair reading or knitting The sum of all such naps may amount to several hours and compensates in part for the shorter nocturnal sleep

Insomnia when it is unrelated to the aging process as such should be treated as in younger patients, by attempting to correct its causes and by the discreet use of soporifics If the lessened sleep of advancing years does not cause weariness and irritability the patient should learn to accept the

shorter hours as normal and adjust his living to this new nocturnal habit When such sleep is insufficient for the individual soporifics may be given phenobarbital 1½ gr or some other barbiturate or chloral hydrate 10 to 15 gr It is best to avoid the constant use of these drugs and to give them only when they are really needed

SMOKING

In the later years of life as in youth smoking does less harm than is generally believed If a person has smoked with impunity up to the age of 50 he will rarely be injured by tobacco in the declining years of his life Moderation is desirable Ten cigarets or two or three cigars daily should be sufficient Tobacco is harmful when smoking immediately gives rise to such symptoms as precordial pain palpitation dizziness and digestive disturbances In such cases smoking should be prohibited Patients with peripheral vascular disease must eliminate smoking completely because there is no doubt that tobacco exercises a harmful effect on the progress of the disease The bronchitis accompanying emphysema is perpetuated and aggravated by smoking With these exceptions elderly persons may be allowed to smoke in moderation As a matter of fact older persons usually voluntarily cut down their tobacco consumption because they begin to lose the taste for smoking or have persuaded themselves that it gives rise to some discomfort or hope that by such abstention they may prolong their lives

tongue with absent papillae may reflect a lack of the pellagra preventive factor nicotinic acid In mild cases the tip and lateral margins of the tongue are reddened and swollen In more severe cases there are intense glossitis stomatitis and gingivitis The tongue is red swollen and smooth There may be secondary infection with Vincent's organisms Petechiae or hemorrhages into the skin in adults rarely point to vitamin C deficiency in the presence of jaundice or serious impairment of intestinal absorption they may indicate lack of vitamin K Rarely a pellagra like eruption may reveal a serious nutritional disorder

Skin and mucous membranes—The skin should be inspected for its elasticity and dryness The presence of senile keratoses should be observed particularly in sites where continuous irritation may give rise to malignant metaplasia The toenails in old people are often thick and irregular and may lead to excoriations of the skin which favor infection Large calluses on the soles of the feet may cause distress Varicose veins should always be sought for The state of the teeth should be studied from the point of view of infection apical abscesses and pyorrhea as well as in regard to their efficiency as chewing organs

Eyes—Conjunctivitis is common presbyopia almost universal and glaucoma and cataract occur often enough to be kept in mind The eyegrounds should be examined to discover the condition of the arteries and to detect possible hemorrhages or exudates which may point to serious hypertension or diabetes

Ears—Impairment of hearing especially for high tones increases with advancing years Today this can be compensated for by appropriate electric hearing devices

Lungs—Pulmonary emphysema is common in older people It may cause dyspnea and cyanosis in the absence of heart

disease and predisposes to recurrent attacks of bronchitis The emphysematous chest is usually characterized by elevation and rigidity of the ribs with calcification of the costal cartilages and a gentle kyphosis of the spinal column A chronic cough and equivocal lung signs should not without further investigation be accepted as evidence of chronic bronchitis Indolent pulmonary tuberculosis occurs with sufficient frequency in older persons to make it necessary to search for it in every case Lung tumors should always be thought of when cough and chest pain develop for the first time after the age of 50 Physical signs may be scanty and confusing The most common signs are those of atelectasis

Lymph nodes —Enlarged lymph nodes in old persons are often evidence of tumor metastasis Nodes in the left supraclavicular fossa may indicate cancer of the stomach supraclavicular nodes may represent extensions from the mediastinum or lungs and axillary nodes from the breast or the lungs Multiple lymph node enlargement may be the result of lymphatic leukemia or lymphosarcoma

Heart —The symptomatology is of more importance than are the physical findings in determining the integrity and the reserve power of the heart Since coronary artery sclerosis is the most frequent cause of cardiac disorders in the aged inquiry into symptoms of angina pectoris takes first place The physician should further question in regard to dyspnea orthopnea and cough Headaches and vertigo in a hypertensive may point to the danger of a cerebral vascular accident The pulse should be felt not alone in the radial arteries but also in the femoral posterior tibial and dorsalis pedis arteries for circulatory impairment in the extremities is common In doubtful cases oscillometric readings should be made of the arterial pulsations in the legs The discovery of arteriosclerosis in the peripheral arteries does not justify the

inference that the visceral and especially the coronary or cerebral arteries are similarly affected for the distribution of arteriosclerosis in the body follows no uniform pattern Of course the routine physical examination of the heart should be carried out An electrocardiogram should be taken of every person over 50 who comes for a health inventory or who has symptoms that are at all suggestive of cardiac impairment Often this will reveal an unsuspected myocardial lesion The blood pressure should always be measured

Gastro intestinal tract —Here too the symptomatology is more important than the physical examination If one waits for palpable tumors to appear it is too late A story of newly developed indigestion or epigastric discomfort especially when associated with loss of weight should always arouse the suspicion of gastric carcinoma particularly in men A sudden change in bowel function either constipation or intermittent diarrhea calls for investigation of the colon for possible neoplasm Roentgen examination of the stomach and colon as well as gastroscopy or sigmoidoscopy should be employed promptly when there is the slightest question of malignancy in the gastro intestinal tract Chemical test of the stool for blood or determination of the sedimentation rate of the red blood cells may offer valuable confirmatory evidence Regulation of the bowels and control of gas is a major problem in older patients A rectal examination should never be omitted It may reveal a latent rectal carcinoma or an enlarged prostate In the presence of hemorrhoids never assume that bleeding is due to the hemorrhoids alone There may be another more serious lesion as well

Genito urinary system —The commonest disorders of this organ system in the aged are prostatic enlargement with difficulty in micturition in men and cystocele with faulty bladder control and cystitis in women In a man with en

dence of obstruction of urinary outflow the volume of resid ual urine should be measured in order to determine the degree of obstruction and the type of treatment that is indi cated Renal insufficiency due to nephritis or contracted kid neys is not so common The most valuable test of renal function is the determination of specific gravity of the urine A low fixed specific gravity is the best indication of kidney insufficiency and unless this is present blood nitrogen studies are unnecessary The urine should be tested for sugar

Skeletal system and joints—Disproportion between the weight of the body and the weight carrying capacity of the feet often leads to static disturbances in the joints of the lower extremities A heavy pendulous abdomen associated with a lumbar lordosis causes back pain Heavy pendulous breasts may cause higher dorsal pain Postural defects loss of muscle tone and obesity are responsible for many of the joint pains of older persons Osteo arthritis of the spine is common in older people and the degree of change found by roentgen examination does not correspond to the symptoms that may arise from disorders of the spine Patients with extensive hypertrophic changes may have no symptoms and those with minimal visible lesions may have great disablement Infectious or rheumatoid arthritis occurs but is rare in elderly individuals It is most unusual to relieve such a con dition by discovery and removal of a focus of infection The physician should always keep in mind that gout may be responsible for arthritic symptoms in older persons A careful history may disclose ancient typical gouty attacks and in spection may reveal tophi in the ears or gouty deposits in the olecranon bursa or along the tendons of the fingers Obscure bone pains should always suggest metastatic neoplastic depos its in the bones Roentgen study and determination of sedi mentation rate and serum phosphatase are then indicated

Central nervous system—Tremor as the first evidence of Parkinson's disease is the symptom most commonly encountered In the early stages there may be nothing but a slight tremulousness of the thumb Absent knee jerks and pupils fixed to light should direct a search for cerebrospinal syphilis but these signs may occur in diabetics or severe arteriosclerotics in the absence of syphilis

Blood—A hemoglobin determination with an instrument that gives accurate readings is indispensable because the color of older persons is highly deceptive Secondary anemia may be the first intimation of a serious systemic disease or of inadequate diet Polycythemia most commonly is secondary to advanced pulmonary emphysema The sedimentation rate of the red blood cells is a useful test An accelerated rate gives evidence of serious organic disease that must be uncovered

Fever—The patient's temperature should always be taken by rectum The mouth temperature in the aged may give a deceptively low reading either because of slowed circulation in the mouth or because the patient cannot keep his mouth closed The skin of old persons with fever often does not feel very warm because of the lessened vasomotor response in the cutaneous blood vessels Commonly old people show less of a rise in temperature than do the young and bronchopneumonia may run its course with no or very little febrile reaction

Pain—It is claimed that elderly individuals experience pain less readily than do the young In my experience this has not been the rule except in severely debilitated persons with dulled sensoriums Within one week I saw three patients aged 72 77 and 85 suffering from severe pain of acute cholecystitis from acute anginal pain accompanying coronary thrombosis and from intense pain in the wrists resulting from acute infectious arthritis respectively

Some principles of diagnosis—The discovery of a lesion

particularly in an older person does not necessarily mean that that lesion is responsible for the symptoms of which the patient complains Gall stones occur in over 10 per cent of women over the age of 45 and their discovery by roentgen examination is often accidental The physician must establish a logical connection between such a lesion and the symptomatology before ascribing the disease condition to that lesion I have seen neoplasms of the stomach and colon overlooked because the patient happened to have gall stones Similarly dyspnea in an older person with hypertension and some cardiac enlargement should not automatically be ascribed to heart failure it may be caused by emphysema or some other pulmonary process A rapid pulse rate in such a patient may be due to hyperthyroidism it does not always connote heart failure

The unitary principle of diagnosis the principle that one diagnosis must be found that will explain all of the lesions and symptoms does not always apply in the case of chronic diseases in older persons In these patients there is frequently a simultaneous derangement of several organ systems and a too rigid adherence to the principle of unitary diagnosis which applies primarily to young people with acute diseases may lead the physician astray Men with coronary artery disease commonly suffer from peptic ulcer and occasionally from gastric carcinoma hyperthyroidism not rarely is associated with organic heart disease lung tumors are found in patients with pulmonary tuberculosis In his diagnostic study of older persons the physician should always keep in mind these possibilities and should not hesitate to seek multiple causes for symptoms that cannot be simply interpreted Frequently two conditions—heart failure and pulmonary emphysema—contribute to such a common complaint as shortness of breath and the relative importance of each of these factors

in causation of the symptom should be carefully evaluated.

Treatment.—Some reference has already been made to the principle that, as far as possible, the elderly patient's habitual routine of life should not be disturbed and that he should be helped and encouraged to remain a useful member of society. At times radical forms of treatment are necessary, such as operations for cancers or prostatic obstruction, or complete bed rest for severe heart failure, or amputation of a limb for gangrene, but, by and large, the physician does best who treats his elderly patients with conservative methods.

Bed rest.—The deleterious effects of bed rest on aged persons are well known. It induces loss of muscle tone with wasting of the muscles. There is a remarkable loss of calcium from the skeleton; the calcium excretion may increase by as much as 400 per cent. The resulting calcinuria may be sufficient to cause formation of renal calculi. Bed rest further leads to urinary retention and aggravation of prostatism, constipation and loss of appetite. Pulmonary congestion and bronchopneumonia are common. These hazards have been excellently described by Laplace and Nicholson[1] who studied 30 patients with hip fractures. One half of those between the ages of 65 and 83 died. Careful studies revealed that these old patients begin to fail during the second, third and fourth weeks of immobilization. Because of their decreased muscle function and loss of muscle tonus, there is peripheral blood stasis and blood accumulates in the venous capillaries and venules. As a result, the circulating blood volume is reduced, and peripheral vasoconstriction follows. These vascular reactions are similar to those that occur in shock. The resulting poor peripheral circulation causes local tissue anoxemia and

[1] Laplace, L. B., and Nicholson, J. T. "Prolonged Recumbency as a Contributory Cause of Death in Elderly Persons," J. A. M. A. 110:247, Jan. 22, 1938.

necrosis Decubitus ulcers are common there is absorption of toxins from these infected areas The patient shows progressive apathy toxic psychoses may develop and there is commonly a terminal bronchopneumonia Thrombosis of the veins of the pelvis or of the lower extremities occurs and pulmonary embolism may result

If old people have to be kept in bed great care should be taken to shift their position frequently and to have them move about in bed as much as possible Practically the only exception to this rule is in patients with severe heart failure Systematic muscular exercises and massage, particularly of the lower extremities must be carried out Especial attention should be paid to care of the skin Many old persons can sit up in a chair for at least part of the day Even walking to the bathroom or similar mild activities are beneficial. Convalescence from bronchitis or bronchopneumonia from operations or even from heart failure may be hastened by such partial mobilization In addition to activating the peripheral blood pumping action of the voluntary muscles it promotes the pulmonary circulation by favoring excursions of the ribs and diaphragm

Surgery—Operation should not be withheld from anyone for reasons of age alone With proper selection of cases with careful preoperative preparation and with meticulous operative technic operations on elderly persons do not offer an undue risk to the patient When there is a true emergency such as acute appendicitis incarcerated or strangulated hernia or obstructive lesion of the bowel there can be no debate operation offers the only means to save life There are many disease conditions amenable to surgical correction that make life miserable and the patient will gladly take a certain risk to gain relief from his discomfort. Typical examples are prostatism very large hernias cataract and certain

forms of gallbladder disease In each individual case the surgeon must weigh the several factors involved the urgency of the situation from the point of view of saving life, the possibility of relieving serious discomfort and of prolonging life the general physical condition of the patient, his mental attitude and the life expectancy of the patient as compared to the operative risk Actual experience of many able surgeons has shown that the operative risk among the aged is not prohibitive and that many individuals have their lives prolonged and their existences made comfortable by well planned and executed surgical procedures

At the Mayo Clinic[2] in the years 1939 and 1940 1 364 operations were done on 1 204 patients aged 65 years or over with an operative mortality of 9 per cent In those aged 65 to 74 the mortality was 8 per cent in those 75 to 79 it was 13 per cent In those over 80 it was 35 per cent In emergency operations such as those for repair of an incarcerated or strangulated hernia and acute appendicitis it ranged from 30 to 20 per cent and interventions to relieve intestinal obstruction had a mortality of 70 per cent Major operation for benign disease showed a total mortality of 7 per cent and for malignant conditions 8 per cent for operable lesions and 16 per cent for inoperable lesions These are encouraging figures They emphasize the gravity of emergency operations and suggest the advisability of correcting remediable defects earlier in life when it can be done with little risk This applies particularly to hernias and to diseased gallbladders that give rise to persistent or recurrent symptoms

The advisability of operation is determined in large measure by the general condition of the patient Undernourished dried out pale individuals are poor operative risks as are the

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[2] Wilcox L E and Clagett O T Surgical Procedures on Patients of Advanced Age Proc Staff Meet Mayo Clin 16 795 Dec 10 1941

fat and flabby In the case of the aged an additional guide is his mental attitude—his will to live Every candidate for operation should be subjected to a painstaking physical examination An evaluation of the heart should determine the adequacy of the cardiac reserve and the degree of coronary artery sclerosis The symptoms are as important as the physical findings Dyspnea cough edema indicate a poor cardiac reserve Angina pectoris points to serious involvement of the coronary arteries The more readily the anginal seizure comes on the poorer the surgical risk Patients with coronary disease may develop cardiac infarction postoperatively The unexpected mortality from this complication is about 5 per cent Shock and hemorrhage are particularly prone to induce such an incident Hypertension without serious cardiac complications does not add much to the hazards of operation The size of the heart as determined by fluoroscopy is a useful guide The larger the heart the poorer the cardiac reserve The quality of the heart sounds gives valuable information as to the state of the heart muscle A dull feeble first sound usually indicates myocardial impairment a loud forceful first sound suggests a strong heart muscle An electrocardiogram should be taken routinely before operation Extrasystoles are rarely of serious import Auricular fibrillation or partial or complete heart block indicates cardiac impairment The presence of demonstrable coronary artery disease of calcareous aortic stenosis of great cardiac enlargement of auricular fibrillation or of symptoms or signs of heart failure gives evidence that the patient is a poor operative risk In such cases operation should be undertaken only if there is a clear cut indication and if the underlying disease will lead to still further cardiac damage or early death

Pulmonary emphysema and fibrosis and chronic bronchitis favor the development of postoperative pneumonia Such

pneumonias occur with particular frequency among the elderly They can often be prevented by careful anesthesia and by the routine preoperative employment of sulfadiazine or of penicillin The usual doses of one of these preparations should be administered for two days before the operation and continued postoperatively until every chance of pneumonitis is past

Kidney function should be tested in every case A simple measure is the concentration test If the specific gravity of the urine rises above 1 020 the kidney function is fairly adequate if it remains between 1 015 and 1 020 there is impairment of renal function Specific gravity that remains below 1 015 indicates serious renal damage Determination of the urea nitrogen of the blood gives further information In men the condition of the prostate gland should be investigated preoperatively not alone because prostatic obstruction may have led to renal injury but because even patients with early prostatic hypertrophy may postoperatively experience difficulty in urination or transient complete retention of urine

A complete blood count should be carried out preoperatively Secondary anemia is common in the elderly

In all but emergency cases every effort should be made to restore the patient to his optimum condition before operation is undertaken If he is undernourished he should be fed carefully for several weeks It is well to supplement the diet with liberal doses of vitamins especially of the B complex In the presence of anemia iron should be administered, and if this does not suffice to restore the hemoglobin resort should be had to transfusion If there is heart failure the cardiac reserve should be built up with rest and digitalis Similarly the reserve power of the damaged kidney should be restored as far as possible Even mild bronchitis is a contraindication to operation

Anesthesia —The administration of anesthesia should be entrusted to a skilled anesthetist and adapted to the individual case The routine preoperative use of morphine is unwise it is too great a respiratory depressant A dose of 1/6 gr should rarely be exceeded Ether is probably the safest anesthetic in the hands of the inexperienced It is well tolerated by patients with heart disease For those with pulmonary emphysema and chronic bronchitis it is too irritating to the air passages and should not be employed In such cases cyclopropane is preferable With this agent induction of anesthesia is rapid and smooth and recovery is rapid A high concentration of oxygen can be maintained so that there is reduced danger of anoxia With high concentrations of cyclopropane cardiac irregularities may occur These should be avoided If greater relaxation of the patient is needed curare may be administered intravenously while the patient is only lightly anesthetized with cyclopropane [3] Spinal anesthesia is useful for operations on the prostate gland and on the lower extremities A small dosage of the drug is usually sufficient and this prevents the drop in blood pressure that accompanies the higher spinal anesthesias Sudden lowering of blood pressure is hazardous to older patients particularly to those with hypertension or with cardiac impairment Intravenous anesthesia with sodium pentothal may be employed in selected cases, but not for abdominal surgery or for operations lasting more than 45 minutes This drug may cause respiratory depression in the aged so that the induction of anesthesia should be slow and the total dose kept small—not in excess of 1 to 1 5 Gm

Postoperative complications that occur with particular frequency among elderly patients are bronchopneumonia

[3] Knight R T and Baird J W "Anesthesia for the Aging and Aged Journal Lancet 64 183 1944

thrombosis of the peripheral veins and pulmonary embolism, cardiac infarction and psychoses Early mobilization of the patient is one of the best means of preventing most of these untoward events The position of the patient in bed should be frequently changed and he should be compelled to flex and extend his legs at frequent intervals If he is unable to move his legs massage should be given twice daily He should be allowed out of bed at the earliest possible moment

Chapter Five

DISEASES OF THE CARDIOVASCULAR SYSTEM

PREVALENCE

DISEASES of the heart have become the leading cause of death with a death rate of 269 per 100 000 This rate includes persons of all ages With each decade after 40 cardiovascular diseases loom ever greater as causes of illness and death In the decade 40 to 49 heart diseases are responsible for about 25 per cent of all deaths With each succeeding decade they exact a greater toll Forty per cent of persons between the ages of 50 and 59 52 per cent of those between 60 and 69 62 per cent of those between 70 and 79 and 66 per cent of those between 80 and 89 die of a heart disease Thus a knowledge of heart diseases is a major requirement for the physician treating persons of advanced years

The phenomenal increased prevalence of heart diseases has led to the inference that some factors in our present civilization and way of life are responsible for it It has been suggested that the hurry and strain of modern living and the increased urbanization and industrialization of our population bring about an early wearing out of our cardiovascular apparatus Careful studies have demonstrated that this is not the case The incidence of heart diseases in age groups under 40 has actually decreased due to the lessened incidence of

rheumatic fever and its sequel rheumatic heart disease In the older age groups the increase in frequency of heart diseases as a cause of death is of about the same magnitude as the decrease in infectious diseases (diseases such as pneumonia and tuberculosis) in these same age periods Escaping infectious diseases we live long enough to develop one of the heart diseases Increased accuracy of diagnosis particularly in the field of coronary artery disease and certain changing fashions in diagnosis contribute to the apparent increased frequency of heart diseases Thus the diagnosis senility" has largely been eliminated and replaced by diagnosis of a cardiovascular condition The increasing prevalence of heart diseases is due to the fact that we are living longer and are less subject to the infectious diseases It reflects in fact favorable influences in the health of the people

Aging of the Heart and Arteries

The concept is erroneous that diseases of the heart and arteries at ages past 50 are inevitable manifestations of the aging process that they are unavoidable and incurable [1] The changes in structure and function of the heart and arteries that come with age are few and simple and do not give rise to clinical syndromes of disease nor do they lead directly to death The important senescent changes in the heart are pigmentation of the heart muscle fibers atrophy of the heart muscle enlargement of the valvular ostia and stretching and loss of elasticity of the valves The electrocardiogram of the aged has no characteristics that distinguish it from that of younger persons There is an increasing tendency to left axis deviation an increase in the relative duration of systole and

[1] Boas E P Aging of the Cardiovascular System Bull New York Acad Med 16 607 October 1940

a lessened frequency of sinus irregularity Prolongation of the PR interval is common Studies have shown that about one quarter of persons over the age of 70 who are presumably normal have electrocardiograms indicative of myocardial damage These abnormal electrocardiograms however are evidence of arteriosclerotic myocardial disease not of aging

The arteries and veins become elongated and dilated from the progressive deterioration of their elastic tissue and there is some thickening of the intima The aorta serves as an example of the behavior of the large elastic arteries As it grows older the aorta experiences a slow progressive loss of elasticity This process begins in the third decade and becomes accelerated after age 50 It is due to changes in the elastic properties of the elastic fibers in the media which lose their coil like undulations and fail to re coil when they are stretched In addition microscopic studies show an increasing fine calcification of the media of equal degree in both sexes that develops rapidly after the age of 20 and is universal after age 50 The intensity of the calcium deposit is a function of the age of the aorta [3] In youth the area of its cross section in the contracted state is relatively small but it can be expanded to three or four times its resting size With advancing years the cross sectional area becomes progressively greater with ever less capacity for distention [4] This change in size and elasticity of the aorta bears no relation to the presence of arteriosclerosis

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[2] Wilens S L "The Postmortem Elasticity of the Adult Human Aorta Its Relation to Age and to the Distribution of Intimal Atheromas" Am J Path 13 811 1937

[3] Blumenthal H T *et al* "Calcification of the Media of the Human Aorta and Its Relation to Intimal Arteriosclerosis Aging and Disease Am J Path 20 665 1944

[4] Wintemitz M C *et al* *The Biology of Arteriosclerosis* (Springfield Ill Charles C Thomas Publisher 1938)

Simple intimal thickening is evidently a physiological process for it begins in the first years of life and occurs regularly in all but the smallest muscular arteries Thickening of the intima after the fourth decade is due to increase of collagenous tissue and shows fatty hyaline and calcific changes as well It gives rise to the typical picture of arteriosclerosis

The maximum blood flow through the coronary arterial tree is about 35 per cent less after the age of 60 than in youth[5]

Changes in function of the heart and arteries occur with advancing years The pulse rate remains fairly constant until about age 65 when it tends to increase to a slight degree The cardiac output per square meter of body surface measured under basal conditions declines very slightly in old age This decline results largely from the lessened oxygen consumption of the body

The idea that with increasing age there is a progressive rise in blood pressure still finds general acceptance The term hypertension is employed far too loosely True arterial hypertension which so commonly leads to cardiovascular disease is characterized by an elevation of both systolic and diastolic blood pressures Systolic hypertension without rise in diastolic pressure has an altogether different mechanism and is the result not the cause of cardiovascular disturbances The common form of hypertension met with in the aged is a systolic hypertension In the later decades of life the systolic blood pressure may rise to about 140 or 160 mm of mercury while the diastolic pressure remains unaltered[6] This systolic hypertension and increase in pulse pressure is not caused by a narrowing of the peripheral arterial bed and does not place

[5] Dock W "The Capacity of the Coronary Bed in Cardiac Hypertrophy" J Exper Med 74 177 September 1941

[6] Miller I "Blood Pressure Studies in the Aged" New York State J Med 41 1631 Aug 15 1941 Russek H I *et al* "Influence of Age on Blood Pressure" Am Heart J 32 468 October 1946

an added strain on the heart and arteries it is the result of the loss of elasticity and the increased atherosclerosis and rigidity of the aorta and large arteries The increasing length and width of the aorta and large arteries compensate for their loss of elasticity and help to keep the internal tension of the aortic wall constant The increase in systolic pressure in the aged is an expression of loss of arterial elasticity and in its effect on cardiovascular dynamics is a beneficent reaction

A hyperactive carotid sinus reflex manifested by temporary cardiac standstill and fall in arterial tension following pressure over the common carotid artery at its bifurcation is more frequent in advanced age especially in men The hyperactive reflex is commonly encountered in patients with arteriosclerosis of the carotid or of the coronary arteries It may be the cause of syncope

Although the functions of the cardiovascular system undergo relatively slight changes with advancing years the circulatory system is not as competent as it was in youth The aged make less demand on their hearts they eat less their physical activity is greatly lessened they avoid extremes of cold and heat and they are unaware that their hearts have become weaker for they have little need for the cardiac reserves that they had in their youth Under basal conditions the functioning of the heart and arteries suffices to meet the needs of the body but the circulatory system like the rest of the aging organism has lost its resiliency and the power of quick adaptation to changing external stimuli When outward circumstances compel aging individuals to take the buffetings of life as they did when they were younger they discover that they lack adaptability they cannot respond to the stresses of a physically active life

In order of their importance the conditions responsible for diseases of the heart and arteries in older persons are

arteriosclerosis arterial hypertension syphilis rheumatic valvular disease hyperthyroidism

Arteriosclerosis

Arteriosclerosis may involve any of the arteries of the body It gives rise to clinical symptoms of disease when it seriously impairs the blood supply of certain vital organs in particular the heart the brain the kidneys or the lower extremities. The cause of arteriosclerosis is unknown Certain observations suggest that dietary and metabolic factors may be important in its genesis but knowledge is insufficient to permit prevention Smoking physical and emotional strain cannot be regarded as causes of arteriosclerosis Although the earliest evidences of arteriosclerosis are encountered on the autopsy table in youth clinical evidences of arteriosclerosis are uncommon before the age of 40 Their frequency increases up to about age 70 After this age the incidence seems to be lower for persons who survive the seventh decade apparently are born with stronger and more resistant blood vessels. Hereditary influences are commonly observed in the occurrence of arteriosclerosis More than one member of a family is usually afflicted, and in certain families every member succumbs to arterial disease when he arrives at a certain age Arteriosclerosis is about four times as common in men as in women Diabetes favors the development of arteriosclerosis, so that diabetic women suffer from arteriosclerotic manifestations as frequently as do diabetic men

Pathology —Arteriosclerosis is an all inclusive term applied to several distinct forms of arterial disease One should differentiate calcification of the media or the Mönckeberg form of arteriosclerosis occurring chiefly in the arteries of the extremities arteriolosclerosis of the small arterioles of certain

viscera of patients who have been subject to long standing hypertension and atherosclerosis which is the common form of lipoid infiltration of the intima with atheroma formation seen classically in the aorta and larger arteries

The Monckeberg type of arteriosclerosis involves the muscular arteries particularly those of the extremities and occurs predominantly in males who are past middle life It is most common in the femoral artery between Poupart s ligament and the popliteal fossa The anterior and posterior tibial arteries are frequently involved the radial artery less often The calcium deposits begin in the interstitial substance between the muscle fibers but soon coalesce to form plaques and bands that encircle the artery In the fully developed form the vessel feels like a goose trachea In later stages bone formation may occur in the calcified areas Calcification of the media does not lead to intimal thickening or to narrowing of the arterial lumen It therefore does not give rise to symptoms of disease It is easily visualized by roentgen examination

Arteriolosclerosis represents the reaction of the small arterioles to the strain of a long lasting hypertension It occurs chiefly in the arteries of the kidney pancreas spleen and liver It is characterized by a subendothelial hyaline deposit and degeneration which gradually narrow the lumen of the vessel There may be fatty infiltration of the hyaline deposits and secondarily there is increase in connective tissue cells and collagen The muscle of the media atrophies as the intima becomes thicker In the larger arterioles there is hyperplasia of the internal elastic membrane As a result of the progressive narrowing and closure of the arterioles of the kidney glomeruli and tubules become atrophic and fibrous and the end result is the granular contracted kidney

Atherosclerosis manifests itself at first as delicate yellowish flecks in the intima caused by deposits of cholesterol esters in

the interstitial substance and cells of the intima It occurs in the aorta in children and in the anterior descending branch of the left coronary artery in many young adults Gradually this fine granular lipoid deposit increases and accompanying it there are swelling of the cement substance and development of collagenous material in the subendothelial layer *Thus a localized swelling or plaque of the intima is formed* There follows a connective tissue reaction which some believe is caused by the cholesterol deposits and layer upon layer of connective tissue may overlie the area of infiltration This new tissue may undergo subsequent lipoid change Eventually the deeper areas of lipoid infiltration undergo atheromatous degeneration and free cholesterol crystals are *deposited in the arterial tissues Calcification may follow* or the atheromatous softened area may ulcerate into the lumen of the artery Thrombi may form on the ulcerated surface As a result of these complex changes the lumen of the artery may be greatly narrowed or completely obliterated Hemorrhages commonly occur within the arterial wall about an atheromatous area and such a hematoma of the artery wall *may further narrow the lumen*

It is believed that the primary factor in atherosclerosis is a molecular change of the intima *with imbibition of blood* plasma and a deposit in the intima of cholesterol esters from the blood plasma Certain mechanical factors play a role in determining the site of these arterial changes for they occur in those portions of arteries exposed to stress or in regions *where fixation of the vessel impairs its expansile mobility* Thus the earliest lesions in the aorta occur near the origin of the intercostal vessels the abdominal aorta which is fixed against the spine is more involved than the thoracic portion patches of arteriosclerosis occur chiefly on the posterior wall of the aorta and by predilection at the sites opposite the upper

and lower borders of the bodies of the vertebrae Moschcowitz[7] has emphasized again the role of intra arterial tension in the genesis of arteriosclerosis and its development in the pulmonary artery when the tension of the lesser circulation is increased Winternitz[8] has stressed the fact that the distribution of the vasa vasorum is related to the occurrence of arteriosclerotic plaques

All the evidence suggests that arteriosclerosis is a disease not a degenerative process of senescence If arteriosclerosis were a phenomenon of senescence it should be encountered with some degree of uniformity in arteries throughout the body it should appear with some measure of regularity and with similar frequencies among persons of different races and in the two sexes Experience shows that this is not the fact Arteriosclerosis and particularly coronary sclerosis is far less common among Negroes than among whites It is very rare among the natives of northern China That arteriosclerosis occurs less often in women than in men is known to all clinicians and pathologists In women with hypertension coronary sclerosis is frequently encountered Sclerosis of the pulmonary arteries is far less common than sclerosis of the systemic arteries and when it is well developed there is almost invariably some process such as mitral stenosis or extensive pulmonary disease that has led to increased pressure in the pulmonary circulation In diabetics the percentage mortality from arteriosclerosis is one third greater than for the population as a whole and women are affected as frequently as are men In children widespread advanced arteriosclerosis is encountered in the presence of severe

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[7] Moschcowitz E *Vascular Sclerosis* (New York City Oxford University Press 1942)

[8] Winternitz M C Thomas R M and LeCompte P M *The Biology of Arteriosclerosis* (Springfield Ill Charles C Thomas Publisher 1938)

nephrosis In hereditary xanthomatosis a condition characterized by xanthomatous nodules and a high blood cholesterol level arteriosclerosis is the rule and sudden death from coronary occlusion common

These observations clearly indicate that arteriosclerosis is not a simple wearing out of the arterial coats that comes with age but that it is a disease a disease it is true that manifests itself mainly but by no means exclusively during the period of senescence It remains a challenge to scientific investigation and a problem for constructive therapy

HEART DISEASE DUE TO SCLEROSIS OF THE CORONARY ARTERIES

Pathology —The degree of sclerosis may vary from a slight fatty deposit in the intima to extensive involvement of the vessel wall with calcification ulceration and obliteration of the lumen The sclerosis may be diffuse affecting most of the larger and smaller branches and giving rise to pipestem arteries or it may be localized An atherosclerotic plaque less than 1 cm in length may completely close the lumen although the rest of the artery may appear healthy Slow closure of an artery from arteriosclerotic narrowing favors the development of a collateral circulation so that when the affected vessel is finally obliterated by a thrombus no infarction of the myocardium may take place The development of collaterals is the rule in patients with coronary artery sclerosis and explains how they survive successive closures of different branches of the coronary arterial tree Hemorrhages are often found in the wall of a coronary artery around atherosclerotic areas The resulting swelling of the arterial wall may cause occlusion of the vessel or the hemorrhage may provoke the formation of a thrombus



FIG 2 —*Above* thrombosis of a coronary artery *Below* section of the myocardium through a recent infarct The infarct appears yellow streaked with red

which will occlude the lumen at the site of the hemorrhage

When a thrombus forms suddenly in a large coronary artery which has not been narrowed for a length of time sufficient to allow the development of collateral channels infarction of the myocardium takes place Infarcts are found most commonly in the anterior wall of the left ventricle near the apex in the papillary muscles of the left chamber and in the upper posterior portion of the left ventricle A recent infarct represents an area of necrosis of the heart muscle It has a soft consistency and slowly in the course of four to eight weeks is replaced by scar tissue which eventually becomes firm Over the endocardial aspect of the infarct mural thrombi commonly form on the pericardial aspect a reactive pericarditis occurs Emboli may be released from the mural thrombus and may find lodgment anywhere in the peripheral circulation most frequently in the arteries of the brain of the extremities or of the kidneys At times rupture of the heart through the softened infarct leads to sudden death

Aneurysm of the ventricle results when a large area of heart muscle has been destroyed and replaced by a relatively thin sheet of fibrous tissue This area then bulges in systole and may gradually increase in size

Coronary arteriosclerosis gives rise to disturbances of cardiac function when the impairment of blood flow to the myocardium is sufficient to cause anoxemia of the heart muscle Commonly the coronary blood flow is adequate with the body at rest but with exertion the diseased vessels cannot accommodate the needed greater flow of blood When such inadequacy is transient the patient experiences typical anginal pain which passes away when with rest the call for a greater blood flow is passed If the exertion is more severe anginal pain may be prolonged and when the disproportion between the blood flow and the blood need of the myocar



Fig 3 —Aneurysm of the left ventricle

dium is sufficiently great actual myocardial necrosis or infarct formation can take place even without coronary occlusion This condition is referred to as coronary insufficiency Spasm of the coronary arteries may contribute to insufficiency of a coronary circulation already impaired by arteriosclerosis The most common cause of reflex coronary spasm is cold This explains the instantaneous onset of angina pectoris in many patients when they step out of the house on a wintry day Reflexes arising in the gastro intestinal tract or gallbladder may also induce coronary spasm Emotion and anxiety are common causes Thrombosis of one coronary artery induces spasm in other branches These reflexes are mediated by the vagus nerve and can be minimized by the employment of full doses of atropine When as a result of repeated coronary closures and advanced coronary sclerosis myocardial damage has been extensive heart failure may occur Under such circumstances cardiac hypertrophy may develop even in the absence of hypertension

ANGINA PECTORIS DUE TO CORONARY ARTERY SCLEROSIS

Angina pectoris is rarely encountered in patients below the age of 40 It becomes increasingly common in the fifth sixth and seventh decades but after age 70 is less in evidence It occurs about four times as often in men as in women In women it is commonly associated with diabetes and hyper tension It is a common complication among older diabetics Angina pectoris is seen less frequently among Negroes than among whites

Symptoms—The presenting symptom is a pressing con stricting breath taking pain experienced under the sternum and brought on by some form of physical activity or emo tional stress The pain is of such intensity and the sense of

being unable to breathe so great that the patient is compelled to stand still until the distress wears off in a few minutes The actual site where the pain is experienced varies greatly The substernal location is the commonest but frequently it is felt just to the left of the sternum and commonly it radiates to the back of the left shoulder and down the inner aspect of the left arm However the pain may be felt in the right chest anteriorly in the back between the shoulder blades or at times in the epigastrium Radiation may be to the right arm or to the neck and jaw In some persons pain is not a prominent feature these complain of a choking sensation and inability to breathe The most characteristic features of the anginal attack are that it comes with effort induces immobility and is relieved by rest Any pain above the waist that has these characteristics is suspect of being anginal in nature In the anginal attack there is usually no change in the heart rate or in the blood pressure although at times there is a transient elevation in pressure Anginal attacks are provoked more readily by walking after a meal or in cold windy weather or when the patient is hurrying under stress and tension The anginal syndrome may come on insidiously at first appearing only under great effort Gradually through the years the pain comes more often and on less provocation In other cases the onset is sudden A man who has been feeling perfectly well suddenly experiences his first anginal attack while walking or while shoveling snow or dancing This may be quite severe and may last about 15 minutes He recovers promptly but from that time on effort always produces anginal pain usually of less intensity than that experienced with the first attack In these cases it is clear that the sudden onset must have been associated with some immediate permanent change in caliber of a coronary artery such as a hemorrhage into a coronary arterial wall In other

cases anginal symptoms first appear after a frank coronary thrombosis

Gastro intestinal symptoms are a common feature of the anginal attack The patient complains of epigastric oppression or fullness and often finds that belching relieves both the abdominal and precordial distress A hiatal hernia may cause symptoms simulating those of angina pectoris (see p 305) There are interesting associations between angina pectoris and peptic ulcer [9] The symptoms of peptic ulcer and anginal symptoms may develop suddenly and simultaneously and occasionally acute peptic ulcer may be associated with coronary thrombosis Attacks of angina pectoris may occur at rest two or three hours after meals and during the night at the hours characteristic of pain from ulcer Epigastric localization of anginal pain may be conditioned by a preexisting peptic ulcer When symptoms of angina pectoris and peptic ulcer coexist successful treatment for the symptoms of ulcer may induce remission of the anginal syndrome The common denominator of the two syndromes seems to be heightened excitability of the vagus mechanism Symptoms of peptic ulcer may arise from vagal activity in the stomach and symptoms of angina pectoris may result from vagal coronary vaso constriction A functional disturbance of one organ may reflexly via the vagus nerve induce a disorder in the other

Physical examination is usually unrevealing Hypertension occurs in only one half the cases In the absence of hypertension the heart is not enlarged Usually the heart sounds are of good quality No murmurs are heard except in cases of calcareous aortic stenosis which may also give rise to the anginal syndrome Sclerosis of the peripheral arteries or of the arteries of the retina may or may not coexist The pres

[9] Levy H and Boas E P Angina Pectoris and the Syndrome of Peptic Ulcer Arch Int Med 71 301 March 1943

ence of sclerosis in one artery does not permit the inference that other arteries in the body are similarly affected for the intensity of the arteriosclerotic process in different parts of the body may be quite unequal The electrocardiogram is often normal Only when previous closure of a coronary artery with resultant cardiac damage has taken place are electrocardiographic changes encountered The electrocardiograms may take any of the forms seen with myocardial disease

Diagnosis —The diagnosis is based chiefly on the history for in classic cases there may be no abnormal physical or electrocardiographic signs So the symptomatology must be inquired into with great care One should ascertain the mode of onset and duration of the pain as well as its site, its character and radiation Precordial pain is a common complaint Benign precordial pain which does not connote coronary disease is felt about the apex it is often sharp and sticking or it is a dull continuous distress It is not provoked by exertion but often comes at rest in bed or after a heavy day's work It does not compel the subject to stop in his tracks In women this type of pain is especially common even when associated with hypertension it need not indicate coronary artery disease Angina pectoris is rare in women under the age of 50 and in women up to the age of 60 it is unusual unless there is associated hypertension or diabetes In older women it is not uncommon Nerve root pains caused by spondylitis may be felt in the precordium They occur at rest or with movement of the trunk At times gall stone colic may cause confusion The diagnosis of angina pectoris is confirmed by the history of a past coronary artery thrombosis or by the discovery of an abnormal electrocardiogram

Prognosis —The prognosis for angina pectoris due to coronary artery disease is difficult to give for the individual case By and large it is much more hopeful than was thought 10

years ago Many of these patients live for 10 to 20 years without significant change in their status Yet there is an element of uncertainty in every case Sudden death or coronary thrombosis may occur at any time Whereas the patient should be given the hopeful point of view, some member of the family should be told that although things may go well for a long time a serious complication may occur unexpectedly the next day the next week in a month or in a year The more readily the attacks come on and the more easily they are induced the graver the prognosis When there are many attacks a day and when attacks occur at rest the outlook is much more serious for in such cases a coronary occlusion may be expected at any time These cases are discussed in further detail in the following section on coronary insufficiency

MANAGEMENT

Prevention —Coronary artery disease cannot be recognized before it manifests itself by symptoms except in rare instances when a routine electrocardiogram may disclose evidences of myocardial injury Yet it is most desirable to recognize disease of the arteries of the heart at the earliest possible moment for there is ample evidence that coronary artery thrombosis is often induced in such diseased vessels by unusual stress or strain In men over the age of 40 any pain in the chest neck arms jaws or epigastrium induced by physical activity should arouse suspicion and call for careful examination including electrocardiography The more carefully one enters upon the history of each individual case the more often does one find symptoms that in the light of subsequent events can be recognized as those of angina pectoris Or one discovers that a sudden effort or emotional strain was followed by an aggravation of symptoms or by a true coronary

thrombosis In such individuals the occurrence of coronary thrombosis can often be postponed if the diagnosis is made early and if appropriate measures are taken It is wise too in older men to take routine electrocardiograms before subjecting them to the strain of a major operation

Treatment—Although it is impossible to influence the progress of arteriosclerosis or to bring about a regression of lesions already existing treatment can give much relief and prolong life Therapeutic efforts should be centered on the patient rather than on the diseased heart or arteries Should the patient be told the true nature of his disorder? The terms angina pectoris and hardening of the arteries of the heart are so well known to the laity and strike such terror in *their* hearts that it is rarely wise to employ *them* The patient is too apt to recall the case of a friend or relative or some prominent individual who died suddenly from coronary artery disease Yet the patient should be informed that his heart is injured for only with such knowledge can he take care of himself properly Whenever possible it is best to use some general expression such as heart strain or to explain that the heart is slowly losing the elasticity and responsiveness of youth and that it must be spared If the patient guesses the truth the physician should take pains to explain that many patients with coronary artery disease even after a thrombosis live long lives and that with care they may look forward to many years of fruitful activity It is appalling how careless many physicians are in pronouncing diagnoses that without qualification terrify the patient Unfortunately many go still further and either in their attempts at making the patient slow the tempo of his life or else for fear that they will be censured for overlooking a serious lesion in case the patient dies suddenly inform him that he has a serious heart lesion and that at any time he

may fall dead Every year I see many individuals who have been so frightened by their physicians that the psychic dis organization provoked by their fears outweighs by far the symptoms of their disease It is essential to paint the picture as brightly as possible while guiding the patient to realize that his future depends largely upon himself At the same time the physician should take some member of the family into his confidence and explain more fully the nature of the disease But here too emphasis should be placed on the uncertainty rather than on the fatality of the condition Many may live for years but death or serious invalidism may occur at any time

Treatment as in all cases of heart disease calls first for the regulation of the patient s activities and reference may be made to the principles laid down for the treatment of patients with essential hypertension In the case of sufferers from angina pectoris there is a more certain guide to activity and that is the anginal pain itself The patient must learn so to control and adjust his daily routine that it does not give rise to anginal attacks The appearance of pain is always an in dication that the heart has been overtaxed If by slowing the tempo of his activities the patient can go through the day without anginal attacks the routine of his life should not be interrupted There is no evidence that in the ordinary case the complete interruption of physical activity with the adop tion of a state of semi invalidism serves to prolong life It certainly leads to hypochondriasis and psychic and moral deterioration This is observed most strikingly in patients who have sufficient disability insurance to enable them to live on the proceeds These unhappy individuals learn to live for their hearts alone are always apprehensive and never at ease They are constantly searching for symptoms arising in the heart This state of mind is subconsciously furthered by the

knowledge that demonstrable disability is necessary for a continuance of the disability benefit

Whenever possible therefore, the patient should be kept at his work It may be necessary to curtail the hours of work or the intensity of his activities but so long as he can go through the day without distress he is far better off busy than idle Many physicians are afraid to allow their patients to work for fear that if they suffer a major seizure while at work the doctor will be censured for permitting them too great activity It is my conviction that aside from instances of definite acute overstrain physical activity or inactivity bears no relationship to the progress of coronary artery disease and that attacks of coronary thrombosis are just as apt to lay low the patient who is endeavoring to conserve his strength at home as one who has resumed his normal occupation This point should be explained to the patient s family In the case of men who are engaged in heavy manual occupations change of work should be insisted on Yet it is astonishing how many of them through force of necessity continue on their jobs for many years without serious distress The physician should be guided by the reaction of the patient As soon as it is evident that a daily routine or particular form of activity gives rise to symptoms the disturbing factor should be eliminated Slow measured physical activity during a full working day does less harm than do sudden spurts of exertion Lifting a heavy object running to catch a bus shoveling snow on a cold winter day partaking of a heavy meal and intense emotional excitement often precipitate acute cardiac infarction Such activities should never be undertaken

Exercise for its own sake should be avoided although short leisurely walks of a mile or so may be permitted All games as well as swimming should be prohibited Although many patients with angina pectoris can play golf without distress

it is wiser to prohibit this activity too Bathing not swimming may be allowed in the absence of surf when the water and air are warm Driving an automobile is usually well borne unless the patient is a nervous tense driver He should be warned again hurry and should try to avoid situations in which a sudden severe pull on the wheel or other forcible action is necessary Of course he should not be allowed to change tires or endeavor to make any other heavy repairs In the average case there is little danger that the patient will die suddenly at the wheel before he can bring the car to a stop

There is no one diet that benefits all patients with coronary artery disease Obesity calls for reduction in weight The point of importance is to eat lightly never to permit a sense of epigastric fullness after eating At times it is better to take five small meals rather than the conventional three meals a day Foodstuffs which the patient has learned by experience cause gas or epigastric distress should be avoided Anginal attacks are provoked most readily by physical exertion on a full stomach The patient should make it a habit to rest in an easy chair for one half hour to an hour after every meal Many patients experience their only pain on leaving the house early in the morning after breakfast They should have breakfast early enough so that they can relax and read the newspaper before leaving the house

When angina pectoris occurs at rest two or more hours after meals it may be due to relative hypoglycemia Harrison and Finks[10] have shown that although blood sugar values at such times may be only slightly subnormal symptoms can often be relieved by the administration of sugar and reproduced by the injection of insulin Patients with such peri

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[10] Harrison T R and Finks R M Glucose Deficiency as a Factor in the Production of Symptoms Referable to the Cardiovascular System Am Heart J 26 147 August 1943

odicity of anginal attacks often find permanent relief from a diet poor in carbohydrate and high in protein with supplementary feedings between meals

Patients with the combined syndromes of peptic ulcer and angina pectoris should receive a modified Sippy diet with frequent feedings In addition they should receive full doses of atropine enough to induce dryness of the mouth i e from 1/150 to 1/75 gr three or four times a day One third to 1/2 gr of phenobarbital given three times a day lessens reflex excitability In some cases alkalis or colloidal aluminum hydroxide may be useful

Although anginal seizures are at times provoked by sexual intercourse complete abstinence often has a worse effect upon the patient He should be taught to avoid sexual excitement but when he feels the need he should have normal sexual relations

Smoking in moderation may usually be permitted There are certain few patients who can relate their cardiac pain directly to smoking These must give up the use of tobacco completely but the majority of patients with angina pectoris are not harmed by smoking 10 to 15 cigarets or a few cigars daily Recent suggestions that coronary artery disease is determined by an allergic response to tobacco are as yet unproved

Alcohol in moderation promotes relaxation and often exerts a beneficial effect in these patients

Medication —Nitroglycerin is the one invaluable drug in the treatment of angina pectoris It is purely symptomatic in its effect relieving the pain of the acute attack most probably by dilating the coronary arteries It is of no value when given several times a day in the hope of preventing attacks If certain activities such as defecation or the first walk on leaving the house in the morning regularly induce anginal seizures nitroglycerin taken immediately beforehand may

prevent the onset of pain The patient with angina pectoris should always carry with him tablets of nitroglycerin and take one promptly at the first signs of genuine precordial oppression The tablet should be placed under the tongue and allowed to dissolve there The usual dose is 1/100 gr *which may be repeated if necessary as soon as the effects of* the first dose have worn off Some patients develop severe throbbing headaches from this dosage and for them 1/150 gr may be sufficient Amyl nitrite in the form of pearls that are crushed in a handkerchief allowing the patient to inhale the volatilizing fluid is equally efficacious but is more likely to cause headaches Since we are seeking an immediate transient effect these two preparations of the nitrites are the ones preferred Sodium nitrite and erythrol tetranitrate are slower in their action and are more apt to be followed by severe headache Given three or four times a day in ½ gr doses they are useful when anginal attacks are very frequent

There still is controversy as to whether the purine derivatives such as aminophylline and theobromine relieve coronary spasm and improve the circulation of the heart I have rarely if ever seen benefit from these drugs when given orally and not infrequently they cause gastric disturbances Theobromine sodium salicylate may be given in doses of 5 to 15 gr three times a day and aminophylline in a dosage of 1½ to 3 gr three times a day There are many proprietary modifications of these purine derivatives that have no particular virtues over the two drugs that have been cited These preparations usually contain a sedative as well and owe their effects largely to this Large doses of aminophylline given in a manner that permits rapid absorption of the drug often do prevent recurrent anginal seizures At least 7½ gr should be given intravenously or preferably by rectum in the form of a suppository or by instillation of the powder dissolved in

water The dose may be repeated several times a day Some patients do not tolerate the drug because of irritation of the rectum or the occurrence of nausea Various muscle and pancreatic extracts as well as testosterone propionate have been recommended under the supposition that they will promote dilatation of the coronary arteries These too I have found of little value

When anginal attacks are related to the onset of extrasystolic irregularity the abolition of the arrhythmia by the use of quinidine sulfate may bring about a striking increase in the capacity to work without pain The dosage of quinidine sulfate for this purpose is 3 gr three or four times a day

Potassium iodide is of no benefit

Next to nitroglycerin the most valuable drugs in the treatment of angina pectoris are the sedatives Phenobarbital in a dosage of ½ gr three times a day is probably the most widely used although all of the barbiturates are equally effectual In some cases particularly when there is arterial hypertension 5 gr of chloral hydrate and 10 gr of sodium bromide taken three times a day bring considerable relief When the attacks are chiefly nocturnal the patient should take an early very light evening meal and a full dose of the sedative before going to sleep

Surgery —Operative treatment is indicated chiefly in patients who develop anginal attacks on the slightest effort and who do not improve under strict medical treatment The various forms of cervicothoracic sympathectomy are attended with an operative mortality of about 21 per cent although they at times give relief They have been largely abandoned and properly so Equally good results with much less risk can be achieved by injecting small quantities of 95 per cent alcohol paravertebrally into the upper four or five thoracic posterior ganglia This procedure interrupts sympathetic

pathways from the heart to the spinal cord This method was first suggested by Mandl[11] and elaborated by Swetlow[1] and White[13] Injection of the posterior ganglia is difficult and should be done by a surgeon skilled in the technic who does paravertebral injections frequently In many instances dis turbing painful intercostal neuritis which may last several months develops after the injection If the injection has been skillful the relief of anginal pain is immediate and usually permanent

A systemic disturbance that burdens the heart with in creased work may make manifest a latent coronary arterio sclerosis by provoking cardiac pain on slight exertion Re lieving the heart of this unnecessary strain may lead to com plete disappearance of symptoms of angina pectoris at least for a time Such a combination is found in hyperthyroidism and in severe anemias In both conditions the heart labors to maintain an increased minute volume flow The immediate indication is relief of the systemic disturbance In patients with hyperthyroidism and angina pectoris subtotal thyroid ectomy is urgently indicated and is usually well borne Many hesitate to operate but there is no other recourse and delay usually leads to disaster In severe anemias the heart com pensates for the diminished oxygen carrying power of the blood by making it circulate faster Restoration of the blood to normal relieves the heart of this extra work In hyper chromic anemia treatment with liver extract brings speedy relief The secondary anemias encountered in patients with

[11] Mandl F Weitere Erfahrungen mit der paravertebralen Injektion bei der Angina pectoris Wien klin Wchnschr 38 759 1925

[12] Swetlow G I Angina Pectoris Paravertebral Alcohol Block for Relief of Pain Am J Surg 9 88 July 1930

[13] White J C Angina Pectoris Treatment by Paravertebral Alcohol In jection or Operation Based on Newer Concepts of Cardiac Innervation " Am J Surg 9 98 July 1930

angina pectoris that are amenable to treatment are usually due to continuous or repeated bleeding as from hemorrhoids or fibromyomata The bleeding must be stopped, by operation if necessary and the blood picture restored by the administration of large doses of iron At times preliminary transfusion is helpful This can be done without danger if citrated blood is given slowly by intravenous drip so that the flow can be regulated at will

CORONARY INSUFFICIENCY

When anginal attacks occur many times during the day, and particularly when they occur repeatedly at rest or during sleep the conclusion is warranted that there is advanced narrowing of one or more of the coronary arteries Minimal increases in the circulatory requirements induce cardiac anoxemia because of this extreme interference with coronary blood flow There exists a state of coronary insufficiency In such patients one can predict that a coronary artery occlusion will occur in a short time Rarely patients may continue with innumerable anginal attacks for many months before this event takes place but more commonly it occurs much sooner Physical signs and the electrocardiogram may remain normal until the closure actually takes place

There is another form of coronary insufficiency in which the patient experiences a severe prolonged attack of anginal pain lasting from half an hour to an hour This usually follows some unusual exertion or excitement During the attack these cases are indistinguishable from actual coronary thrombosis but the subsequent course shows that no myocardial infarction has taken place, because no fever leukocytosis or permanent electrocardiographic changes develop during subsequent days Within a few days the patient feels

as well as he did before the attack At times actual myocardial infarction may take place under such circumstances without closure of a coronary artery This occurs particularly when the coronary flow is greatly slowed following shock or hemorrhage *This is the most extreme form of coronary insufficiency* and cannot be distinguished from coronary thrombosis except on the autopsy table

Treatment —Coronary insufficiency with innumerable anginal attacks daily is most difficult to treat The patient should be completely immobilized in bed for many weeks The aim in therapy is to spare the heart every unnecessary strain until a collateral circulation has developed of sufficient degree to take over the function of the vessel that is almost obliterated Nitroglycerin should be used as soon as the patient feels an attack coming on He may take from 20 to 30 tablets a day In these cases sodium nitrite or erythrol tetranitrate in doses of from ½ to 1 gr four to six times a day or 7½ gr suppositories of aminophylline several times a day may reduce the number of attacks If attacks occur during sleep a dose of erythrol tetranitrate should be taken just before retiring Sedatives should be given freely Often these measures do not halt the attacks and recourse must be had to codeine and morphine Papaverine in ½ gr doses may be useful These patients suffer so greatly that one is tempted to do almost anything to give them relief Indeed they beg that some drastic measure be carried out Yet in such cases it is very risky to proceed with paravertebral alcohol block The shock of this operation may readily induce a coronary closure The diet should be very light and very small in quantity In these cases the prescription of an 800 calorie diet is indicated It lightens the work of the heart during digestion and if persisted in for four weeks reduces the basal metabolic rate and so indirectly spares the heart If under this

regimen attacks diminish in frequency and intensity, the patient may gradually be granted increasing activity Far more often, even during strict treatment, a coronary occlusion occurs

CARDIAC INFARCTION AND CORONARY THROMBOSIS

The clinical manifestations of coronary thrombosis are actually the result of cardiac infarction Infarction is caused most often by a thrombus occluding a coronary artery but it may be due to coronary occlusion from any cause thrombosis embolism hemorrhage into the arterial wall or rupture into the lumen of an atheromatous abscess in the arterial wall Infarction may result from prolonged coronary insufficiency without arterial occlusion, as may occur in shock or hemorrhage Coronary thrombosis may occur without subsequent cardiac infarction if there is a rich collateral coronary arterial circulation In such a case the patient may manifest the classic initial symptoms of coronary thrombosis but recovers within 24 hours without developing fever electrocardiographic changes or other evidences of myocardial infarction The discussion of cardiac infarction in the following pages includes consideration of the syndrome of coronary thrombosis

Cardiac infarction may occur at any time in a patient suffering from angina pectoris It may also strike without warning a person who has had no previous symptoms of heart disease Not infrequently certain prodromal symptoms may give warning of an impending attack some days before it actually occurs In patients with angina pectoris as has been pointed out the occurrence of frequent attacks at rest indicates the imminence of a coronary closure The sudden onset of anginal attacks at rest or an unusually prolonged attack after some effort usually indicates that a coronary closure is



Fig 4 –Infarct of the anterior aspect of the left ventricle Arrow indicates intraventricular thrombus

on the way Several days or a week may elapse during which there are repeated lesser attacks of pain without sequelae until finally a major seizure indicates that infarction has taken place

Although many times a cardiac infarction may occur without evident cause in a large proportion of cases the onset of symptoms can be traced to a definite unusual event in the patient s life [14] The most frequent cause is some severe bodily effort such as pushing an automobile out of a ditch or some exceptional strain while at work Physical exertion in cold weather is especially prone to cause attacks Every winter I see several men who develop their first symptoms while shoveling snow or while struggling through snow drifts Overeating and overdrinking at banquets and weddings particularly when followed by dancing is a common antecedent story In other cases drinking large quantities of iced drinks may precipitate an attack Sexual intercourse as well as unusual emotional excitement may be a direct cause of cardiac infarction Infections such as influenza and pneumonia and operations in patients with coronary disease are commonly followed by cardiac infarction

The clinical picture of a major cardiac infarction is well known The patient is seized with an agonizing constricting substernal pain and feels as though the chest were being compressed by a heavy weight the pain may radiate down one or both arms or up the neck He becomes tremendously apprehensive and breaks out in a cold sweat Symptoms of shock appear The blood pressure drops the pulse becomes feeble and thready Some die in the acute attack but in most cases there is slow recovery from the shock particularly after morphine has been administered In some the pain subsides

[14] Boas E P "Some Immediate Causes of Cardiac Infarction" Am Heart J 23 1 January 1942

in the course of an hour in others it may persist with gradual lessened intensity for 24 hours With recovery from shock the patient feels fairly well but tremendously weak from the terrible experience he has been through His appearance if first examined at this time may be very deceptive His color is good the pulse slow the heart sounds of good quality and the blood pressure back at its former level After 12 to 24 hours myocardial necrosis begins Absorption of autolytic products of the softening infarct provokes a constitutional reaction *and the damage to the heart muscle becomes ap parent* The temperature rises It may range from 101 to 104 F and gradually recedes in from five to seven days There is leukocytosis which may reach between 12 000 and 20 000 At the same time the pulse becomes rapid the first heart sound becomes dull and if damage has been severe there may be gallop rhythm with accentuation of the second pulmonic sound In about 10 per cent of cases a pericardial friction rub becomes audible This friction rub is very in constant and may come and go within a few hours Rarely it persists for several weeks The blood pressure drops Nor mal blood pressure may be reduced to 90/60 and in a pa tient with previous hypertension figures almost as low may be observed In severe cases congestive heart failure becomes manifest chiefly by dyspnea and moist rales in the lower lobes of the lungs In the severest cases there may be early pulmonary edema Cardiac irregularities may occur Most common are frequent extrasystoles There may be auricular fibrillation With massive infarction of the posterior aspect of the left ventricle there may be partial or complete heart block If the patient survives these irregularities disappear within a few days The electrocardiogram usually gives evi dence of cardiac infarction within a few hours of its occur rence The two classic pictures are those of anterior infarc

tion with a high take off of the T wave in leads 1 and 4 which changes in the next few days and shows Q waves and negative T waves in leads 1 and 4 and those of posterior infarction in which initially there is a high take off of the T wave in leads 2 and 3 followed by the development of Q waves and negative T waves in leads 2 and 3

Death from ventricular fibrillation or rupture of the ventricle may occur at any time during the first weeks after a myocardial infarction If the patient improves there is gradual recession of all of the signs and symptoms However the first heart sound may remain dull and the blood pressure may remain low In cases with severe myocardial damage evidences of heart failure may persist Between the fifth and the fourteenth day after infarction embolism may occur from a thrombus that has formed on the endocardial surface of the left ventricle It may cause a cerebral vascular accident most often hemiplegia it may cause a renal or splenic infarct or the embolus may lodge in one of the arteries of the extremities A large embolus may be arrested at the bifurcation of the aorta giving rise to the clinical picture of the so called saddle thrombus

Commonly myocardial infarction is attended with far fewer symptoms There may be no shock, the pain may be of only half an hour s duration and the constitutional reaction may be slight and transient A patient may experience a true cardiac infarction and return to work after a night s sleep or at most a few days rest in bed Many patients are sent by their physicians to my office for examination within one to seven days after having experienced a cardiac infarction Although many survive such careless handling not a few develop congestive failure because the injured heart has been overtaxed by this inadvisable physical activity I have seen not a few unnecessary deaths in persons who have pursued

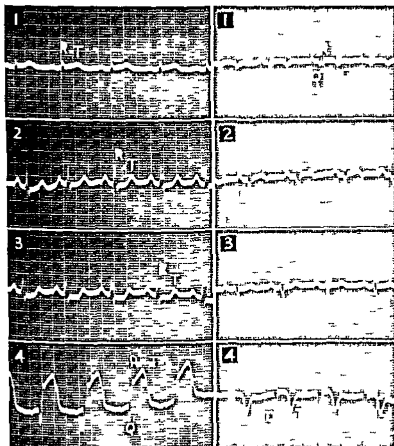


FIG 5—Electrocardiograms *Left* acute infarction of the anterior aspect of the left ventricle note elevation of RT segments and Q waves in leads 1 and 4 *Right* healed infarct of the anterior aspect of the left ventricle Note Q waves and negative T waves in lead 1 and 4

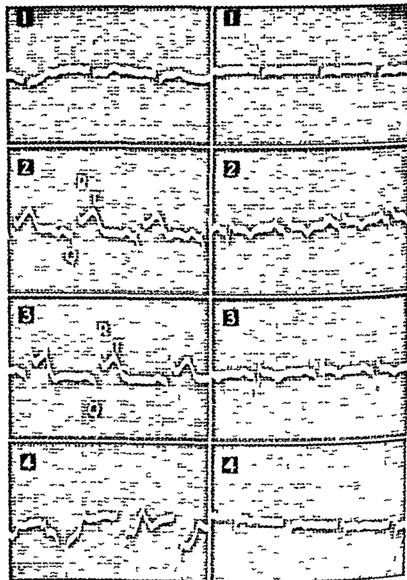


FIG 8 —Posterior infarction of left ventricle *Left* acute infarction (4 hours old) of posterior aspect of left ventricle note elevation of RT segments and Q waves in leads 2 and 3 *Right* healed infarct of posterior aspect of left ventricle (same case) Note Q waves and negative T waves in leads 2 and 3

their normal activities following an unrecognized infarction

The mistaken diagnosis of simple angina pectoris is often made in these cases Anginal pain lasting more than half an hour is almost always followed by cardiac infarction In every such case the physician should assume that an infarction has taken place until it has been disproved Careful recording of the temperature determination of the white blood cell count and the sedimentation rate of the red blood cells will usually lead to a correct interpretation of the clinical picture An electrocardiogram should be taken for positive findings will make the diagnosis certain A normal electrocardiogram however does not exclude the possibility of cardiac infarction

Treatment —Major cardiac infarctions call for prompt and rigorous treatment The patient is in agonizing pain and in shock Large doses of morphine should be given hypodermically It is useless to commence with as small a dose as ¼ gr One half grain should be given at once and if there is no measurable relief within 15 minutes or so another ¼ or even ½ gr should be administered without further delay To lessen reflex spasm in the unaffected coronary arteries atropine sulfate 1/75 gr should be given with each dose of morphine The patient should be put to bed at once He should not be allowed to walk or to help himself in any way but should be carefully carried Any exertion no matter how slight may cause sudden death or precipitate serious heart failure If the patient is very ill it is best not to move him more than is necessary but to make him comfortable wherever he may happen to be The body should not be warmed The cold skin is due to peripheral vasoconstriction a protective device to maintain blood flow through the vital organs

Restlessness calls for more morphine or a sedative such as sodium amytal 3 gr or chloral hydrate 10 to 15 gr The

amount of morphine that may be given can be judged by the degree of contraction of the pupils and by the rate of respiration Usually after 1 gr of morphine the pain is controlled and the patient is fairly comfortable When morphine causes vomiting it should be used sparingly, or dilaudid 1/30 gr may be used instead The shock gradually passes off in one to 12 hours During the first 24 hours following cardiac infarction the patient is suffering from peripheral vascular failure rather than from heart failure Therefore cardiac stimulants should not be given until and unless heart failure supervenes

During the first 24 hours no solid food should be given and only enough fluids to prevent discomfort No attempt should be made to induce bowel movement The patient may not void at all or at most very little This too calls for no interference Because of the state of shock there is actual partial suppression of urine and the kidneys do not resume their normal function for several days

At the end of 24 hours often sooner the acute stage characterized by shock has passed The patient has regained a good color the pulse is full and the blood pressure has risen in part from its original low level Even the heart sounds may have a rather strong quality If the patient has been too ill to be moved to an appropriate place this is the best time to transport him to his home or to a hospital on a stretcher and in an ambulance Then follows the stage of reaction to the cardiac infarct The temperature rises the pulse again becomes weak and rapid congestive rales appear at the bases of the lungs and the liver may become engorged With this the heart sounds become feeble and a pericardial friction murmur may be heard Some pain may persist but it is rarely severe

Pain can be controlled with codeine Half a grain may be

given every four to six hours as necessary Morphine should be used if necessary In addition ½ gr of phenobarbital three times a day helps to promote quiet and relaxation The patient should be kept at complete rest on his back for at least four weeks He should be fed bathed and turned in bed he should not be allowed to do anything for himself The fluid intake should be restricted to about 1 000 cc a day food to about 1 000 calories The diet should be simple and light

No attempt should be made to induce a bowel movement during the first three or four days The effort of defecation or of an enema may overtax the heart If there should be much distention a rectal tip should be inserted but only in case of *absolute necessity should a small enema be given*

If congestive failure appears or if the pulse is rapid and there is gallop rhythm treatment should be directed to the heart In the absence of such signs no specific cardiac medication is necessary Heart failure no matter whether it occurs immediately or after several days always calls for the administration of digitalis The fear that digitalis may do harm in the presence of an acute infarct that it may cause rupture of the heart or induce ventricular extrasystoles or tachycardia is unfounded If heart failure is severe the patient should be quickly digitalized Four cat units should be given intravenously and at the same time 4 more units by mouth Six hours later 4 more cat units may be given by mouth and 12 hours later another 2 units After this it is best not to exceed a dosage of 2 cat units a day This dosage may be continued for a week and then reduced to 1 cat unit daily The best preparation of digitalis is digitoxin which is commercially available as Purodigin or Digitaline Nativelle in 0 2 mg tablets The initial dose is 5 tablets or 1 mg and this is followed by 1 tablet or 0 2 mg once a day Given in these amounts digitalis can do no harm and is almost always

helpful in combating heart failure Some prefer to use strophanthin intravenously for the initial doses One quarter of a milligram may be given as the initial intravenous dose, and this may be repeated in six hours After this, medication should be continued with digitalis by mouth If in spite of this medication much moisture remains in the lungs and the liver remains swollen 2 cc of one of the mercurial diuretics should be given intramuscularly In the presence of severe heart failure intravenous administration of these preparations may induce pulmonary edema The dose may be repeated in three days if necessary When these measures fail the situation is quite desperate and further medication does not offer much promise Four grains of aminophylline in 10 cc of distilled water may be given intravenously or caffeine sodium benzoate may be given hypodermically in doses of 7½ gr every three hours Adrenalin is not useful in these cases and may cause serious harm

Aminophylline by mouth serves no useful purpose and may upset the patient s stomach Some employ glucose intravenously in the hope of improving the nutrition of the heart muscle I have found it of no value In fact such intravenous medication by increasing the blood volume places an extra strain on the heart and may do harm

If congestive failure is severe and there is much cyanosis and dyspnea the administration of oxygen will ease the burden of the laboring heart and improve the nutrition of the myocardium by supplying it with well oxygenated blood Oxygen is best administered through the B L B mask If the patient cannot tolerate the mask the oxygen tent may be used and if other methods fail the simple nasal catheter can be employed

Sudden death following cardiac infarction may result from ventricular fibrillation Some authors have advocated the

routine use of quinidine sulfate in doses of 3 gr three or four times a day to prevent this eventuality It seems unnecessary to administer this drug in every case but when extrasystoles appear particularly at rapid heart rates it should be given until uninterrupted sinus rhythm has re established itself Auricular fibrillation following cardiac infarction rarely calls for quinidine for as a rule the rhythm spontaneously reverts to normal in a few days It is better in such cases to employ digitalis to slow the ventricular rate

Two of the most serious complications of cardiac infarction are embolism from a mural thrombus overlying the infarct and pulmonary embolism arising from phlebothrombosis in the legs If the formation of such thrombi could be prevented by lessening the coagulability of the blood such embolism might be prevented Dicumarol has been administered to patients with cardiac infarction in the hope of achieving this result Dicumarol retards thrombus formation by de pressing the prothrombin level in the blood Dosage must be carefully regulated by daily checks of prothrombin time of the blood This time should be kept at about 40 per cent of normal The initial dose of 300 mg is given as soon as the diagnosis is made About two days are required for the drug to manifest its action Subsequent doses are given daily after the prothrombin time is ascertained The average daily dose is 75 mg but if the prothrombin time approaches normal the dose should be increased and if it is depressed below 40 per cent the dose should be omitted until the level is higher It is too early to evaluate the usefulness of this drug Any bleeding tendency is a contraindication to its use

The sedimentation rate of the red blood cells is a good indicator of whether or not healing of the infarct is complete When the sedimentation rate has become normal one may

assume that the soft infarct has been fully replaced by scar tissue and that it is safe to mobilize the patient No matter how well the patient appears to be doing he should be kept on his back in bed for a full month If at the end of this period there are still evidences of congestive heart failure if the pulse is rapid and there is gallop rhythm, absolute rest must be continued If the cardiac function is good he may be allowed to sit up in bed and within a few days may spend a few hours a day in a chair Gradually his range of activity may be increased so that at the end of another four weeks he is walking freely about the house He should however avoid all undue strain and take several rest periods during the day At the expiration of two months from the time of the coronary thrombosis complete healing of the myocardium has taken place and cardiac function has been largely restored The patient may be allowed to leave the house and gradually test out his capacity for physical activity The range of freedom that may be permitted is determined by the patient's response to effort The appearance of anginal pain or dyspnea on exertion calls for limitation of activity along the principles laid down in the discussion of angina pectoris

The interpretation of the patient's response to effort after he has experienced a coronary artery occlusion is often difficult He is usually fearful always on the lookout for some sign of cardiac embarrassment He walks and handles himself as though he were some fragile object that might break if used too roughly It is a slow and painstaking task to teach him the balance between sensible caution and irrational timidity The evaluation of his symptoms too may lead to error Sticking precordial pain unrelated to effort is common during convalescence from a cardiac infarction It may be caused by the pull of pericardial adhesions that form so commonly it has no clinical significance and should be

ignored Muscular weakness and ready fatigue often have marked psychic components and may call for the prescription of greater activity There is such danger that these convalescents from a serious cardiac accident may become confirmed neurasthenics that the physician should devote special effort to dissipate their fears and to help them learn the degree of activity in which they may indulge with safety

Many of these patients particulary those who have experienced their first attack of coronary thrombosis recover fully and have no sequelae and no disturbing symptoms They should be encouraged to resume their former occupation unless it is one calling for much bodily labor It is doubtful whether complete retirement and a life devoted to guarding the heart against possible stresses and accidents actually accomplishes its end *Recurrent coronary thromboses seem to* come in those who have reduced their living to a mere existence as frequently as in those who have resumed the usual course of life It is true of course that unusual strain should be sedulously avoided A sudden momentary effort *may do more harm than a year s tempered activity and may* in fact induce a thrombosis in a coronary artery The patient should learn not to push himself to avoid competition to escape the drive to which we so often subject ourselves He should give heed to warnings of fatigue and of anginal pain no matter how slight He should arrange his work so that he can carry on with comfort With these simple precautions the majority of those who have recovered from a cardiac infarction can resume the interrupted thread of their lives

There are others in whom anginal pain on greater or less effort develops or persists after the coronary thrombosis These should be handled according to the principles laid down for the treatment of angina pectoris Still others but

these are few have continuing symptoms and signs of congestive heart failure after the coronary closure The treatment of these is outlined in the following section

Prognosis—About 80 per cent of patients recover from their first cardiac infarction The outlook becomes more serious with each subsequent attack The presence or absence of hypertension does not seem to affect the outlook but marked cardiac enlargement is an unfavorable element It favors the development of heart failure The older the patient the more serious the prognosis The mortality from cardiac infarction becomes greater as each successive decade of life has passed In the individual attack, the early onset of heart failure is an unfavorable sign The severity of the heart failure as well as of the constitutional reaction is also an indicator of the seriousness of the individual attack

MYOCARDIAL FIBROSIS WITH HEART FAILURE

When there have been repeated cardiac infarctions or when the coronary arteries have undergone slow but widespread occlusion diffuse myocardial fibrosis results In time so much of the myocardium is destroyed and replaced by fibrous tissue that the contractile power of the remainder is insufficient to maintain the circulation There may be an aneurysm of the left ventricle Aneurysm of the left ventricle is suggested by a diffuse, forceful visible and palpable apex impulse accompanied by a very faint first heart sound The diagnosis is confirmed by fluoroscopy which reveals a protrusion of the left cardiac border which bulges in systole while the rest of the ventricle contracts In simple myocardial fibrosis the heart is usually enlarged and the first heart sound is faint When the heart begins to fail the pulse becomes rapid and the pulmonic second sound becomes accentuated

The failure is primarily of the left ventricle so that dyspnea and congestion of the lungs are the leading symptoms Commonly attacks of paroxysmal dyspnea or so called cardiac asthma form part of the clinical picture These attacks usually occur at night awakening the patient from sleep They may be quite mild and may be relieved when he sits up for a short time More often they are quite intense with agonizing dyspnea and cold sweat In the severest attacks pulmonary edema occurs and may be fatal Gallop rhythm is a constant sign in this form of heart failure and pulsus alternans is frequently encountered When left ventricular failure is far advanced the right ventricle fails too the liver becomes congested and enlarged the neck veins become full and edema of the legs may develop Anginal pain is unusual after heart failure sets in

In spite of the advanced state of the cardiac lesion treatment of these patients often gives great relief and prolongs life Complete bed rest is essential If the patient has not been taking digitalis the drug should be given in the dosage outlined in the section on cardiac infarction If the patient has been taking digitalis maintenance doses only should be given It is unwise to give more than 1 cat unit daily when dosage is to be continued for a long time The dose may be doubled if believed necessary for a week or so at a time

Successful treatment concerns itself primarily with the water metabolism and effects excretion through the kidneys of the excess water in the body Even in the absence of visible edema this may amount to 10 lb or so The presence of this fluid which is associated with an increased blood volume embarrasses the heart After it has been removed the feeble heart is able to maintain the circulation but only so long as the water balance of the body is maintained As soon as fluid again accumulates in the tissues cardiac distress returns

The importance of maintaining the fluid balance in the body was known to the Ancients Celsus wrote

> It is wise to measure the circumference of the abdomen with a string daily On the following day one must always note whether the abdomen has become larger or smaller because only if the body is becoming thinner are the medicines working It is also wise to measure the fluid intake and the urine of the patient because there is hope for recovery only when the patient excretes more fluid than he takes in [1]

He also advised incision of the skin above the ankles for dropsy and abdominal paracentesis for ascites

Successful treatment hinges on a careful recording of the intake and output of fluid In addition to the water ingested in the form of fluid drinks soup and ice, a large amount is taken with solid food Vegetables fruit, meat in fact most foodstuffs contain large quantities of water Water is excreted through the kidneys through the lungs through the skin as visible and invisible perspiration and through the intestines with the stool Fortunately the amount of water ingested as solid food approximately equals that excreted by the lungs skin and intestines so that for practical clinical purposes it suffices to measure the actual fluid intake and the urinary output These should be measured for every 24 hour period and recorded daily A glance at these figures shows at once whether or not the patient is making any progress The urinary output should always exceed the fluid intake by a few hundred cubic centimeters When the patient is not too ill to stand a better check is obtained by weighing him daily at the same hour Daily fluctuations in weight are due to variations in water retention With these records as guides the physician is prepared to initiate treatment

The fluid intake should be limited to 1 000 cc in 24 hours

[1] Celsus Aurelius Cornelius *De Medicina* B III chap XXI

The Karell diet—800 cc of milk and nothing else in 24 hours —is useful but the need for such rigorous measures has largely disappeared with the introduction of the mercurial diuretics The salt intake should be minimal but it is rarely necessary to prescribe a strict salt free diet A diet containing only 1 Gm of salt daily will induce diuresis and permit the patient to drink larger quantities of water All cooking and baking even of bread must be without salt Such a diet is difficult to prepare and many patients refuse to adhere to it It is very useful when dehydration cannot be achieved by other methods

Diuretics —Ammonium chloride should be given in a dosage of 20 to 30 gr three or four times a day It is conveniently administered in the form of the 7½ gr enteric coated tablet which is well tolerated by the stomach When ammonium chloride is absorbed the ammonia is synthesized into urea and the liberated chlorine ion produces acidosis It is this acidosis which is responsible for the diuresis If the heart failure and edema are not too great these simple measures may suffice to rid the body of its excess fluid and to restore the circulatory balance In the presence of markedly impaired renal function these acid producing diuretics should be used with caution for they may bring about serious acidosis This may be suspected if the breathing becomes rapid and deep and can be verified by measuring the carbon dioxide combining power of the blood

If the edema is massive or if dyspnea is distressing diuresis can be hastened by the administration of one of the mercurial diuretics These act upon the kidney tubules preventing the resorption of water that has been excreted by the glomeruli The best of the mercurials are mercupurin mercuhydrin and salyrgan They may be given intravenously or intramuscularly in a dose of 1 to 2 cc If the patient has veins that

are readily accessible for injection the intravenous method is best for it is painless and the action of the drug is more rapid Great care should be taken to avoid introducing any of the drug into the tissues around the vein for this causes a painful induration that may slough and take weeks to heal When intravenous technic is too difficult it is better to give an intramuscular injection although this may be painful These drugs may be given in suppository form in which they are almost as efficacious as when given by injection However many patients cannot tolerate the suppositories for they may cause severe rectal irritation In patients with chronic water retention the oral administration of these diuretics one tablet three times a day, may maintain adequate diuresis and render injections unnecessary Some patients experience abdominal cramps and diarrhea from the oral dosage The dose of the mercurial may be repeated every three to seven days depending on the degree of water retention Even in the absence of gross edema the active diuresis provoked by these drugs often abolishes dyspnea and leads to restoration of circulatory equilibrium

In old people particularly diuresis caused by administration of a mercurial drug may be followed by intense weakness or by muscle cramps These drugs bring about a great elimination of salt as well as of water and it is the excessive salt loss that is responsible for these symptoms They may be relieved by the administration of salt by mouth The occurrence of such symptoms calls for smaller subsequent dosage of the mercurial Usually a dosage can be found that will be tolerated

In the absence of advanced kidney disease the mercurial diuretics are quite safe Albuminuria alone is no contraindication to their use, for it may be due to passive congestion of the kidneys But when the urine contains many red blood

cells and casts it is unsafe to employ these drugs unless it can be established that there is little kidney damage or no active renal disease When the kidney has lost its concentrating power when the specific gravity of the urine is persistently below 1 012 they should be used with great caution Active dehydration under such circumstances may lead to azotemia and to death from uremia I have observed this sequence on a number of occasions

One of the best diuretics for patients with persistent severe heart failure due to advanced myocardial disease is urea It has two major disadvantages its very disagreeable taste and the fact that it often provokes intense thirst The dose is 1 oz two or three times a day It is best administered in orange juice or beer Under its steady use a urine output of from 2 000 to 4 000 cc can easily be maintained Urea is cheap it can be bought for less than a dollar a pound it is non toxic I have observed many patients who have taken it continuously for several years with uniformly good results While urea is being taken the blood urea nitrogen is usually high it may amount to 50 or 60 mg per cent but this causes no ill effects and is no indication for stopping the drug Once a patient has become reconciled to the taste of the drug and has learned how by its continuous use he can control his dyspnea as well as the distress occasioned by a congested liver he is unwilling to give it up The maintenance dose should be the smallest one that will keep him in water balance The mercurial diuretics may be given to supplement the action of urea but this is rarely necessary except in advanced states of dropsy

Compared to the powerful diuretics that have just been discussed drugs such as theobromine and aminophylline are relatively inactive I rarely find occasion for their use Aminophylline may be given in a dosage of 1½ to 3 gr three

times a day and theobromine sodium salicylate 10 to 15 gr three times a day Their diuretic effect is often short lived

Some patients recover from their severe heart failure and maintain their circulation without the need for further diuresis But there are many who again retain water as soon as the diuresis is stopped They remain chronic invalids Their exercise tolerance is minimal they can walk but little most of them are confined to the house many are bed ridden But as long as diuresis is maintained they are comfortable provided they do not overtax their physical reserves The ultimate prognosis of course is poor Few survive more than a year or two

Success in treating these patients depends on *eliminating* every ounce of excess water from their systems and then keeping them "bone dry" This can best be achieved by watching their weight and noting the minimum weight that can be attained at which they are comfortable The patient *should weigh himself every morning on arising and record* the figures A sudden increase of 3 to 5 lb always indicates water retention and warns of impending symptoms of left ventricular failure The immediate administration of a diuretic will eliminate this surplus fluid and again restore the balance of the circulation Such gain in weight *usually* follows excess physical activity or the ingestion of too much fluid These factors too should be kept under constant regulation With careful supervision using the weight as a guide these patients do remarkably well But the briefest relaxation of vigilance and care results in recurrence of *heart failure*

Attacks of *paroxysmal dyspnea* call for emergency treatment Morphine sulfate at least ¼ gr should be given hypodermically at the onset of the attack If there is associated pulmonary edema that does not at once respond to the opiate *and if the veins of the neck and arms are full phlebotomy*

of 500 cc may be done Usually unless there is associated right heart failure there is no indication for phlebotomy indeed the abstraction of blood is difficult because the veins are empty The intravenous administration of 8 gr aminophylline calcium in 10 cc of water may abort the attack If the patient has not been taking digitalis ¼ mg of strophanthin or 2 to 4 cat units of an appropriate digitalis preparation should be given intravenously This should be followed by rapid complete digitalization

At times the application of tourniquets to the four extremities will serve to diminish the circulating blood volume and act as effectually as a phlebotomy The tourniquets should be applied so as to arrest the venous return but still permit transmission of the pulse wave They may be left on for a number of hours On releasing them care should be taken to do so gradually and to free one limb at a time else the rush of blood that has been pooled in the extremities may overtax the heart Hot water bags and hot blankets should be applied to give warmth to the body for the temperature is usually low Aside from morphine digitalis and aminophylline the best drug is caffeine sodium benzoate 7½ gr which may be given hypodermically every hour or two As an emergency stimulant coramine is at times of value It is only effective when given intravenously when it acts as a powerful stimulant to respiration and circulation Its effect however is fleeting

As soon as the patient has recovered from the acute episode of paroxysmal dyspnea active diuresis according to the methods outlined above should be instituted This will often serve to prevent further attacks Since the introduction of the mercurial diuretics thoracentesis and abdominal paracentesis are rarely necessary but if dyspnea is intense and apparently caused by the accumulation of fluid in the serous cavities withdrawal of this fluid may give immediate relief

Diabetes mellitus is commonly encountered in patients with coronary artery disease The principles of treatment are the same as in uncomplicated diabetes with one exception Too rigorous dieting with a view to maintaining a normal blood sugar concentration or too liberal use of insulin may precipitate arterial thrombosis in the coronary or cerebral arteries or in sclerotic arteries of the extremities The diet should be adjusted to maintain the patient s normal weight and to keep the urine practically sugar free If this can be achieved without insulin all the better If insulin is used care should be taken to avoid doses that produce hypoglycemia for a too sudden or too radical reduction in the blood sugar is often accompanied by attacks of angina pectoris or even of coronary thrombosis Most patients with both diabetes and coronary artery disease are past middle life and the diabetes is relatively mild They often feel better when they excrete a little sugar in the urine than when they are under a too rigid regimen

Periarthritis of the shoulder giving rise to pain in the left shoulder and arm is seen so often in patients with coronary artery disease that the association seems to be more than a coincidence Often the acute inflammation about the shoulder joint occurs within a few days after a cardiac infarction or it may develop weeks later When precordial pain radiates to the left shoulder and arm the left shoulder is apt to be the one involved when radiation is to the right the right shoulder is affected Thus in patients with coronary artery disease we see chiefly periarthritis of the left shoulder in contradistinction to the more common right sided lesion Otherwise the clinical picture does not differ from that in patients with normal hearts

Periarthritis of the shoulder is a loose term that includes several conditions One form is associated with calcific de

posits in the supraspinatus tendon The other common form leads to a frozen shoulder and is due to tenosynovitis of the long head of the biceps and its sheath[16] It may begin with a mild ache in the shoulder which is exaggerated by external rotation The pain and limitation of motion gradually increase and there may be a secondary scalenus spasm that induces pain in the neck and back of the shoulder There is marked limitation of abduction and external rotation Motion may be so restricted that fibrous ankylosis is simulated The full picture may develop quickly The pain is persistent and severe it is exaggerated by movement and lying in bed may be impossible because no weight can be borne on the shoulder Trophic disturbances may appear in the hand and there may be marked atrophy of the shoulder girdle The condition is self limited and gradually after many months clears up completely

Anginal pain often radiates to the shoulder and arm it may be chiefly manifest in this location When such a periarthritis occurs in a patient with angina pectoris the shoulder pain is apt to be severe apparently because the sensory nervous pathways of this region have already been sensitized by the radiation of the pain arising in the heart It is often difficult to determine whether such shoulder pain arises from disease in the heart or in the shoulder If the pain comes on effort and if it is associated with typical substernal pain it is anginal in nature If the pain is continuous and aggravated by movements of the arm if lying or turning in bed provokes severe pain in the shoulder and if on examination there are local tenderness and limitation of abduction and external rotation the pain is not a manifestation of angina pectoris but is due to disease of the structures around the shoulder

[16] Lippman R K Frozen Shoulder Periarthritis Bicipital Tenosynovitis, Arch Surg 47 283 September 1943

joint The close association as well as the differentiation of these two conditions are emphasized because they are so often confused Thus a patient whose heart calls for little treatment is confined to bed or greatly restricted and is erroneously given nitroglycerin for the relief of arthritis

When periarthritis of the shoulder is acute absolute immobilization and the application of wet dressings for a few days are essential Heat is often comforting but it may aggravate the pain which frequently is sufficiently severe to require morphine or codeine Aspirin and aminopyrine often give relief In the earlier stages roentgen therapy may be efficacious As the acuteness of the condition subsides gentle massage and diathermy treatments are beneficial It may take weeks or months for the pain fully to subside At times a maneuver devised by Dr E Libman gives instantaneous relief With the thumb pressure is exerted in the anterior triangle of the neck over the brachial plexus until a spot is found where such pressure reproduces the shoulder pain At this point strong pressure often causing severe pain is exerted for one minute Not infrequently this causes immediate and permanent relief from the shoulder pain The mechanism of this legerdemain is not understood In some cases this procedure is ineffective and in others pain and disability return within a day or two Injection of 20 cc of 1 per cent procaine solution into the muscles about the shoulder at the sites of spots that are tender to pressure may give quick relief

Arteriosclerosis of the Cerebral Arteries

Arteriosclerosis of the cerebral arteries affects the brain much as arteriosclerosis of the coronary arteries affects the myocardium Interference with the blood supply to a portion of the brain causes local anoxemia and loss of function of the

affected area If the anoxemia is very transient no permanent damage ensues but if it is at all prolonged the affected nerve tissues die and an irreversible lesion results As in coronary disease occlusion of a cerebral artery may be due to progressive atherosclerotic narrowing it may be caused by thrombosis superimposed upon the arteriosclerosis or there may be hemorrhage into the vessel wall and into the brain due at times to rupture of miliary aneurysms or there may be embolism Shock and hemorrhage by causing marked prolonged insufficiency of the cerebral circulation may induce cerebral softening without thrombosis of one of the arteries of the brain Cerebral arteriosclerosis and resulting cerebral vascular accidents are by no means confined to patients with hypertension As in the case of coronary artery disease hypertension is found in about one half of the cases Since the symptoms in the hypertensive patients are much like those in patients with normal blood pressure they will be discussed together There has been much dispute whether or not spasm of the cerebral vessels can occur and whether transient seizures of hemiplegia or aphasia are caused by such momentary spasm or by small hemorrhages that are quickly absorbed Probably both conditions occur

Just as attacks of angina pectoris may give warning of impending coronary thrombosis so fleeting disturbances of cerebral function may be manifest some time before the cerebral vascular insult occurs Headaches sudden vertigo and confusional states are not uncommon There may be sudden aphasia or merely an impediment of speech which quickly disappears There may be transient hemiplegia Sooner or later a major attack occurs The symptoms depend on the size of the lesion In the case of hemorrhage the additional factor of increased intracerebral pressure contributes to the clinical picture In the classic severe case there is

sudden loss of consciousness accompanied by incontinence of urine and feces Coma may develop more slowly during a period of 12 hours and be heralded by intense unilateral headache vomiting and increasing mental dulness or confusion Breathing is slow and stertorous and may be Cheyne Stokes in character In fatal cases consciousness does not return breathing becomes more and more labored and rapid and the temperature rises steadily and inexorably often reaching 107 to 108 F just before death The pulse is little accelerated and is strong the blood pressure is often elevated Evidence of paralysis of one side of the body can be elicited by close observation of the patient For the first day or two the deep reflexes are abolished but subsequently they become hyperactive on the paralyzed side and the Babinski sign becomes apparent

In favorable cases consciousness gradually returns usually within 24 hours but I have seen patients recover completely after five days of unconsciousness Within 12 to 24 hours the temperature rises and a leukocytosis occurs Fever lasts from three to seven days and is due to absorption of autolyzed products from the infarcted area in the brain At times the cerebral injury may cause a disturbance of temperature regulation Full appraisal of the extent of the paralysis can be made a few days after the apoplectic seizure Recovery is slow Power first returns to the lower extremity beginning in the muscles of the hip and thigh followed by those of the leg The arm is last to recover and often remains useless even when the patient can walk quite well Under appropriate treatment function in the paralyzed limbs may continue to improve for several months In case of aphasia speech may return promptly or the aphasia may persist in its full extent or only slightly Alexia difficulty in reading is a distressing complaint that often accompanies aphasia

Unconsciousness occurs in only half the cases Often hemi plegia monoplegia or aphasia occurs without disturbance of the sensorium The onset may be sudden or slow In the case of hemorrhage the lesion usually develops rapidly although it may progress in the course of the first 24 to 48 hours The symptoms of cerebral embolism appear suddenly and dra matically In older persons the source of the embolus is al most always a mural thrombus of the left ventricle following coronary thrombosis Rarely it is derived from a vegetation of subacute bacterial endocarditis Thrombosis of a cerebral artery is as a rule slow in development and the resultant symptoms develop gradually in the course of 24 to 48 hours

Changes in the mental capacity and emotional pattern of the patient are variable In many the intellectual powers are unimpaired and the patient may resume his normal life with out any evidences of deterioration One of the most striking examples of such recovery is Louis Pasteur who lived 28 years after having experienced a stroke and who in those years accomplished some of his best work In many how ever there results a deterioration of mental capacity Often there is emotional instability particularly when the lesion involves the thalamus There are episodes of uncontrollable laughter or crying After repeated or extensive cerebral vas cular insults mental deterioration becomes marked giving rise eventually to the picture of arteriosclerotic dementia

Not every cerebral vascular insult gives rise to the classic picture of hemiplegia Some may develop symptoms of pseu dobulbar palsy others that of paralysis agitans Often there is no localizing neurological lesion the symptoms being only those of intracranial damage In many instances there are no major episodes with visible neurological sequelae but rather repeated small apoplexies the nature of which is

often unrecognized [16] There may be fainting or acute vertigo or a sudden severe headache with vomiting The symptoms pass off within a few days and are attributed to indigestion Or the patient may suffer a so called nervous breakdown with extreme weakness and exhaustion Following such attacks he may never again be his former self, he may become irritable forgetful and exhibit marked changes in character or temperament become emotional untidy or suffer from insomnia The true nature of the illness is commonly overlooked because of the rapid physical recovery after such an episode and because of the absence of motor or sensory disturbances The best diagnostic lead is a painstaking history which will reveal that the patient s illness dates from a sudden unexpected seizure such as fainting vertigo or vomiting the time of onset of which can be fixed precisely Such minor cerebral vascular injuries may begin in the fifth decade and there may be years of well being before the occurrence of a second one Sooner or later such apoplectic strokes recur and lead to multiple areas of encephalomalacia with resultant physical and mental deterioration and eventual gross neurologic defects Ten or 20 years may elapse before a major seizure causes death

Treatment —The prevention of cerebral vascular accidents is rarely possible except in certain patients with hypertension When the blood pressure particularly the diastolic pressure becomes exceedingly high and the patient complains much of headache bed rest and one or more phlebotomies of 500 cc may relieve the acute symptoms and tide over the situation for a while Most cerebral vascular accidents result from lesions that cannot be controlled In diabetics too rigid dieting designed to reduce the blood sugar

[16] Alvarez W C "Cerebral Arteriosclerosis with Small Commonly Unrecognized Apoplexies" Geriatrics 1 189 1946

to normal or the administration of doses of insulin that induce hypoglycemia may initiate a cerebral thrombosis

With the onset of an acute cerebral vascular accident the patient should be put to bed If the blood pressure is high and the patient appears plethoric and not anemic a phlebotomy of 500 cc should be done At times the intravenous administration of 4 gr of aminophylline which may be repeated several times a day clears the sensorium and lessens the paralytic symptoms Intravenous administration of 25 to 50 cc of 50 per cent glucose solution may serve to reduce intracranial pressure and give some symptomatic relief If respirations are greatly slowed or Cheyne Stokes in character aminophylline or coramine intravenously and caffeine sodium benzoate in doses of 7½ gr subcutaneously are the best drugs Beyond this treatment consists of careful nursing For the first days the patient will be unable to eat and fluids should be given intravenously or by hypodermoclysis particularly if there is high fever When the patient begins to take fluids or food by mouth great care should be taken to avoid aspiration of food particles which results in bronchopneumonia Bronchopneumonia is common in these patients from aspiration of saliva and mucus It should be carefully watched for and if it appears should be treated as any other case of bronchopneumonia Owing to the incontinence of urine and stool bed sores are apt to develop hence the patient should be kept scrupulously clean and dry At times particularly in elderly men with prostatic hypertrophy there is retention of urine necessitating catheterization

In favorable cases improvement is evident within a week Restoration of function in the paralyzed limbs should always be striven for The one procedure that hastens such recovery more than any other is attempt by the patient at voluntary use of the affected parts As soon as possible therefore the

patient should be urged to try to move the palsied limbs and definite exercises should be instituted Passive movements and massage should be carried out at the same time With the same end in view the patient should be moved out of bed at the earliest possible moment This can usually be done within seven to 14 days after the onset Far too often these patients are kept immobile in bed for one or more months Contractures of the paralyzed limbs develop and subsequent mobilization becomes difficult Recovery of the leg in whole or in part can usually be achieved Improvement in function of the arm occurs less often Aphasia too may clear up but if it persists for a week the outlook is not good Here too painstaking re education in speech brings results and although it will not restore normal speech it may make it possible for the patient to communicate with the outside world

During the recovery period medication is of little value Sedatives may be given when needed In certain patients with persistent mental confusion particularly when there appears to be undernutrition due to a prolonged inadequate diet the administration of 50 mg of nicotinic acid three times a day seems to help clear the sensorium This medication should always be tried in older persons with symptoms of senile psychosis or dementia for in a certain number of cases the mental disturbances are due to a pellagra like dietary insufficiency and not to the cerebral arteriosclerosis

Peripheral Arteriosclerosis and Embolism

Arteriosclerosis of the arteries of the extremities is an important cause of illness and disability in elderly persons It is the only form of peripheral arterial disease that occurs with any degree of frequency Thrombo angiitis obliterans and acute arteritis are rarely encountered after the age of

50 The age incidence and the relative frequency of its occurrence among the two sexes and among different racial groups are the same as for other forms of arteriosclerosis Although thickening and tortuosity of the arteries of the upper extremity and of the temporal arteries are common the lesions rarely lead to arterial closure or symptoms of ischemia The arteries of the lower extremities are commonly affected with such advanced degrees of arteriosclerosis that obliteration occurs with consequent impairment of blood supply to the tissues of the extremities The significant lesion is a collagenous and fibrous intimal thickening causing circumscribed regions of stenosis Thrombi form in these narrowed arterial sections and extend centrally The thrombi become organized and canalized and may undergo subsequent hyaline change or atheromatous degeneration Primary intimal atheroma is not a major feature in the vessels below the level of the popliteal artery This is in contrast to the usual atherosclerotic lesions of the coronary arteries Dissection of the arterial tree of legs amputated for gangrene reveals that in this advanced stage there is always widespread occlusion of many arteries The posterior tibial artery is the one most often occluded then follow in the order of frequency the anterior tibial the peroneal the dorsalis pedis and the popliteal arteries In addition to the intimal and thrombotic lesions calcification of the media often with bone formation is found in almost all cases This is the so called Monckeberg arteriosclerosis It does not directly lead to closure of the lumen It is this medial calcium deposit that makes these arteries visible on the roentgen film

The pathological and physiological disturbance is quite analogous to that which has been discussed in the section on coronary artery disease If the development of the arterial disease is slow collateral channels form that compensate for

the obliterated arteries so that final closure of the diseased artery may lead to no serious consequences If arterial closure occurs in the absence of a competent collateral circulation the tissues that have been deprived of their blood supply die Clinically we then see gangrene of part of the lower extremity This is analogous to the myocardial infarction with coronary closure Closure of an artery of an extremity may be slow owing to gradual progress of the arterial lesion or it may be sudden owing to local thrombus formation or to the lodgment of an embolus

Symptoms arising as a result of sclerosis of the arteries of the lower extremity are caused by an inadequate flow of arterial blood The defective circulation is insufficient to wash away the metabolites that accumulate from muscular contraction and one substance which Lewis[17] calls the "P factor" causes pain when it reaches a certain concentration Just as in coronary disease anginal pain results when the heart muscle is called on for extra work so in the extremities the pain of intermittent claudication occurs on effort when the need for blood of the muscles of the extremities is increased as a result of their use in walking or running The onset of such pain on effort may be insidious over many years or it may be sudden if quick thrombosis or embolism of one of the arteries takes place

Commonly a certain degree of arterial spasm is present in addition to the organic changes in the arterial wall Relief of this spasm may permit sufficient restoration of the circulation in the extremity to lessen or abolish symptoms due to ischemia Arterial spasm however is encountered less often in arteriosclerotic disease of the arteries of the extremities in older subjects than in other forms of arterial disease that occur at younger ages

17 Lewis T Pickering G W and Rothschild P "Observations upon Muscular Pain in Intermittent Claudication" Heart 15 359 1931

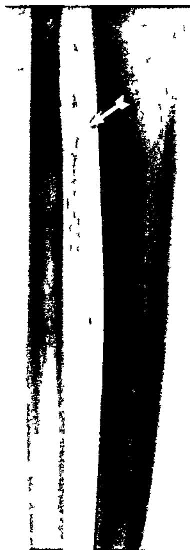


Fig 7—Calcium deposits (arrow) in the arteries of a leg

Symptoms —The presenting symptom of arteriosclerosis of the arteries of the lower extremities is intermittent claudica tion On walking the patient experiences a cramping pain usually in the calf muscles that compels him to stand still After a few minutes rest the pain disappears and walking can be resumed until renewed pain again calls a halt In the early stages this pain comes only on running or on more vigorous exertion but in the course of time it appears more and more readily until eventually the patient may not be able to progress more than half a block before being stopped by the pain Another common complaint is coldness of the legs and feet Such coldness is due to inadequate arterial blood supply to the leg Patients with vasospastic disorders have the same complaint so that this symptom of cold feet should not be regarded as pathognomonic for obliterative arteriosclerosis of the arteries of the extremities Angina pectoris and intermittent claudication commonly occur in the same patient and most often it is the pain in the legs rather than the pain in the heart that actually stops the patient while walking Because of the circulatory disorder in his legs the patient cannot exert himself sufficiently to induce anginal pain Angina in him is provoked by overeating or by emotional disturbances Hypertension occurs in about half the cases As in coronary disease the hypertension seems to accelerate the arteriosclerotic process but it is not its direct cause Diabetes is common in patients with peripheral arte riosclerosis in fact nutritional disturbances of the extremities with gangrene are frequent causes of death in diabetics

When arterial obliteration is far advanced constant severe burning pain may be experienced in the toes or the foot it may be excruciating prevent sleep and yield little to opiates The parts are very tender so that even the weight of the bed clothes may be unbearable and walking or standing impos

sible In an endeavor to find relief the patient may apply a *hot water bag or immerse his foot in hot water and so cause* a serious ulcer or gangrene Ulcers may appear even without such external injuries Gangrene develops as a result of gradual arterial obliteration or following a thrombosis of a diseased artery The favorite sites are the tips of the toes or the heel A spot of purplish discoloration forms which is very *tender Within a few days a black tough dry necrotic eschar* forms In the absence of infection it may persist for weeks before it finally sloughs out leaving a granulating ulcer that takes many more weeks to heal The gangrenous area may gradually spread to involve ever wider regions If it should become infected a condition of so called moist gangrene develops which may extend rapidly up the leg Moist gangrene often develops when pyogenic bacteria enter the lesion of a ringworm infection between the toes

Physical signs —There may be no abnormality in the appearance of the legs When arterial obliteration is advanced the leg appears pale the skin becomes shiny and loses its hair Commonly there are nutritional changes in the toenails which become thickened fissured and brittle Trichophyton infection of the skin and nails is common The local resistance of the tissues is low so that minor cuts and abrasions give rise to slow healing ulcers and infection readily sets in The foot and leg feel cold and one can roughly estimate the extent of the arterial obliteration by noting how high up the leg this coldness extends Palpation of the arteries of the leg discloses whether the pulses are open The physician should routinely palpate the dorsalis pedis posterior tibial and femoral arteries The popliteal artery is difficult to feel When the arteries cannot be felt or when their pulsations are small studies with the oscillometer will give a clear picture of the state of the arterial circulation The oscillometer cuff should

be applied on the thigh on the mid leg and at the ankle Normal readings at the mid thigh range from 8 to 15, at the mid leg from 4 to 10 and at the ankle from 1 to 5 Diminution in the excursion of the oscillometer indicates impairment of the arterial blood supply

A simple clinical test gives further evidence of a reduced blood supply With the patient on his back the leg is elevated to a right angle with the trunk The patient is then instructed to move his toes and ankle vigorously for a few moments The leg becomes very pale almost cadaveric below the level at which the blood supply is impaired The patient then sits up and the leg is allowed to hang down It assumes a dusky bluish red hue Roentgen pictures of the legs may reveal calcification of the arteries This gives no information regarding arterial occlusion for calcification of the media commonly exists in arteries that are patent It is frequently noted in the radial and ulnar arteries However the presence of medial calcification helps to identify the arterial disease as arteriosclerotic in nature for calcification does not occur in thrombo angiitis obliterans Arteriography the injection of a radio paque medium directly into the arteries with immediate roentgen visualization, gives a clear picture of the arterial circulation of the leg and reveals obliterated arteries and the extent of the collateral circulation However it is a difficult technical procedure not without danger It is rarely necessary to carry it out and should be left to experts

Treatment—Great care should be taken to keep the feet and legs clean and free from irritation Shoes should be well fitting to avoid corns The patient should be warned against cutting corns and calluses for infection readily occurs Tightly fitting garters should not be worn Epidermophytosis should be carefully treated Since smoking produces peripheral arterial spasm tobacco in every form must be abso

lutely prohibited Even one or two cigarets daily can do great harm Arterial dilators such as the nitrites theobromine and aminophylline are of no value The intravenous injection of hypertonic salt solution is ineffectual in the treatment of peripheral arteriosclerosis although it seems to help in cases of thrombo angiitis obliterans Intravenous injection of typhoid vaccine which is often useful in thrombo angiitis and in spastic disorders of the arteries should not be employed in arteriosclerosis The treatment is too drastic and may induce acute thrombosis in a peripheral or a coronary artery Various tissue extracts have been employed Given by mouth they have doubtful value Given subcutaneously they at times give relief from intermittent claudication The best preparations are Depropanex and Carnacton Injections may be given every other day Mechanical treatment with the pavaex apparatus that induces alternate suction and compression is of little value Collens claims good results from his intermittent venous occlusion apparatus Surgical methods of treatment such as ganglionectomy should not be employed in patients with arteriosclerotic vascular disease The operative risk is too great Moreover these procedures relieve only the spastic element in peripheral arterial disease and this is not very marked in arteriosclerotic cases Alcohol injection of the peripheral nerves to relieve pain is dangerous in these patients for it may lead to gangrene Application of mecholyl by iontophoresis gives good results in selected cases

In the presence of dry gangrene the patient should be kept in bed and mummification should be allowed to proceed in the hope that spontaneous separation of the dead tissues will take place Even if this does not occur delay gives an opportunity for the development of a collateral circulation and favors better healing of the amputated stump The foot should be placed in a horizontal position elevation further

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amount of collateral circulation and the degree of accompanying myocardial insufficiency Embolism occurs chiefly in patients with heart failure and the inefficient circulation makes the establishment of a collateral circulation more difficult In favorable cases the pain subsides and in the course of 12 to 24 hours color sensation and movement gradually return to the affected part There may be complete recovery If the collateral circulation is inadequate death and gangrene occur in the tissues that have been deprived of blood It may involve just the tips of the toes or the whole foot or leg It is usually a dry mummifying gangrene unless infection is superadded Fever and leukocytosis appear When the embolus is large and is arrested at the bifurcation of the aorta—the so called saddle thrombus—both legs are involved there is absence of femoral pulsation in both legs and gangrene may extend up to the mid thigh If the embolus lodges in the femoral artery gangrene usually extends above the knee when the popliteal artery is occluded death of tissues extends to the mid leg

Ideal treatment is embolectomy—operative removal of the embolus This is not often possible To save the parts distal to the obstruction operation must be performed within 12 hours of the closure The patient is often in poor condition because of the basic heart failure and the shock secondary to the embolism hence the operative mortality is high Moreover it is difficult to localize the embolus In my experience the embolus is always higher than was anticipated Today with the use of heparin to prevent clotting the operative results are a bit better Since approximately half of all patients with embolism to an artery of the lower extremity recover without the development of gangrene and since the operative mortality approaches this same figure conservative treatment is indicated as a rule The affected extremity is

kept at complete rest and is protected against any and every trauma by a cradle baker The temperature within the cradle should be thermostatically controlled between 85 and 95 F For the acute pain morphine should be given In addition it is well to give papaverine hydrochloride in ½ gr doses intravenously every few hours to release the spastic vaso constriction Herrmann has reported good results with the application to the leg of alternate suction and pressure by means of the pavaex apparatus If dry gangrene develops conservative treatment should be continued The part may mummify and eventually drop off It may take weeks or months for this process to be completed particularly if some sequestra of bone must be discharged If a larger area of the leg is involved or if moist gangrene with constitutional reac tion develops amputation becomes necessary Here it is important to gage the time optimum for operation when the heart failure has been corrected as far as possible and the patient has recovered from shock During the interval ab sorption from the gangrenous leg may be reduced by placing the leg in a cuff packed with ice that keeps the temperature near the freezing level

Dissecting Aneurysm of the Aorta

This is a rather rare condition more frequent in men than in women Of the 269 cases collected by Shennan in which ages were known 59 per cent were in persons over the age of 50 although the condition may occur in youth The under lying cause is a cystic degeneration of the media Most of the patients have essential hypertension Usually as a result of sudden physical strain or of excitement there is a rupture of the intima, and blood escapes from the lumen of the aorta into the media It forces its way between the medial

and adventitial coats and may extend down the whole aorta to its bifurcation or spread up the carotid arteries The usual termination is external rupture into the pericardium pleura mediastinum or retroperitoneal region In rare cases the force of the blood dissecting its way between media and adventitia splits the intima again and flows back into the lumen of the aorta If the patient survives as happens in isolated cases he is left with a double barreled aorta for the new passage way has become lined with endothelium Most dissecting aneurysms commence with a transverse irregular tear of the intima in the ascending aorta But the tear may occur lower down even in the abdominal aorta

The symptomatology is characterized by intense pain in the anterior and posterior chest which usually radiates down to the abdomen into the legs In some cases the pain is wholly abdominal The pain is severe and prolonged and does not yield readily to morphine Shock develops and this is followed by fever leukocytosis and dyspnea If the flow into the iliac arteries is blocked the femoral pulses are absent Commonly there is anuria due to closure of the renal arteries This may account for the fact that the blood pressure usually remains elevated The heart sounds remain of good quality and the electrocardiogram shows no typical changes Roentgen pictures of the chest may reveal a marked dilatation of the aorta If the carotid arteries are involved in the process the blood flow to the brain may be stopped and there will be signs of a cerebral vascular insult The condition usually terminates fatally by complete rupture of the aneurysm in from a few hours to several days The average duration between rupture and death is four days Recovery is rare Treatment is confined to administration of large doses of morphine and absolute bed rest

TEMPORAL ARTERITIS

This is a rather unusual self limited disease that manifests itself with fever prostration headache and periarteritis of the temporal arteries[18] All cases so far recorded have been in persons over 50 years of age At the onset the symptoms are not specific There are fever leukocytosis headache pains in the muscles and joints After a few weeks the temporal arteries become tortuous and prominent and tender nodules may appear in the arterial wall Finally the arteries become thrombosed Some of the systemic symptoms are due to involvement of arteries other than the temporals The retinal arteries may be affected and blindness may result Symptoms simulating brain tumor may be due to multiple cerebral arterial thromboses The disease lasts several months and usually ends in complete recovery Its cause is unknown Pathological examination of the affected arteries reveals inflammation with many giant cells of all layers of the arterial wall thickening of the intima and occlusion of the lumen by thrombosis Lesions have been found in many peripheral and visceral arteries[19] There is no specific treatment Resection of a small portion of the involved temporal artery is said to relieve the headache in many instances but it does not shorten the course of the disease

[18] Kilbourne E D and Wolff H G "Cranial Arteritis A Critical Evaluation of the Syndrome of Temporal Arteritis with Report of a Case" Ann Int Med 24 1 1946

[19] Cooke W T *et al* "Temporal Arteritis A Generalized Vascular Disease" Quart J Med 15 47 1946

Chapter Six

DISEASES OF THE CARDIOVASCULAR SYSTEM—HYPERTENSION

MANY older and even aged persons have blood pressures within the range of what clinicians call normal Table 4 modified from Symonds gives the average blood pressures of healthy men and women accepted for life insurance The old idea that the systolic blood pressure approximates 100 plus the age of the patient is incorrect Elevated blood pressure always indicates disease it is not a normal accompaniment of aging

TABLE 4

Age	Men		Women	
	S	D	S	D
50–54	131	86	131	87
55–59	134	87	135	88
60 and over	135	87	136	90

The blood pressure is never static it varies from moment to moment according to the needs of the circulation and the physical and emotional stimuli that are constantly bombarding the vasomotor center During sleep the blood pressure is at its lowest the lowest level during waking hours is reached when the patient is in bed early in the morning before break

fast Exercise and digestion are accompanied by rises in pres sure Emotional stimuli are effective in raising the blood pressure That is why initial readings taken in a physician s office are often so unexpectedly high A subsequent reading taken with the patient relaxed may be 10 to 50 points lower

SYSTOLIC HYPERTENSION

By systolic hypertension is meant an elevation of the sys tolic pressure with little alteration of the diastolic pressure This phenomenon is commonly encountered in old people and is due to a loss of elasticity of the aorta and of the large vessels derived from it The aorta cannot distend to accommo date the volume of blood ejected from the heart it has no give As a consequence with systole the pressure within the aorta suddenly rises steeply the blood is rapidly forced to the periphery so that the pressure rapidly falls and the diastolic pressure is unchanged The blood pressure may range around 150 to 180 systolic and 80 diastolic Systolic hypertension encountered when the aorta is dilated and inelastic and accentuated by extensive atherosclerosis is the result not the cause of a cardiovascular disturbance It does not place an added burden on the heart and does not jeopardize the health or the life of the patient The future of the patient depends on the progress of the underlying atherosclerosis

Systolic hypertension occurs in certain patients with brady cardia The long diastole allows a greater amount of blood to flow from the arteries to the veins the arteries become com paratively empty and consequently the diastolic pressure is low while the systolic pressure is unchanged If the cardiac output per beat is increased the systolic pressure is slightly elevated For instance in a patient with intermittent com plete heart block the blood pressure was 130/85 when the

heart rate was 68 when the rate dropped to 20 the blood pressure was 130/40

Essential Hypertension

Essential hypertension is characterized by elevation of both systolic and diastolic blood pressures The underlying mechanism is a state of peripheral vasoconstriction which retards the flow of blood from arteries to veins and places an increased burden on the heart as well as on the arterial system The consequences of prolonged essential hypertension therefore may be found in the heart which enlarges and may become insufficient and in the arteries which become sclerotic and may give way under strain The arteries of the heart kidneys and brain are chiefly affected and it is in these organs that the complicating lesions in essential hypertension are usually found

In spite of the brilliant work of Goldblatt and his followers in producing hypertension by clamping the renal arteries the true cause of essential hypertension in man has not yet been established Cases in which the hypertension can be directly traced to such an arterial lesion in the kidney and cured by the removal of the kidney are rare Some other factors must be involved In certain kidney diseases the hypertension is definitely the result of the renal disorder The commonest of these diseases is glomerulonephritis which however is uncommonly encountered in older people Hypertension also occurs in periarteritis nodosa with kidney involvement in congenital polycystic kidneys in pyelonephritic contracted kidneys and in some cases of urinary obstruction due to prostatic hypertrophy The kidney lesions in most cases of hypertension are secondary to the hypertension The long standing blood pressure elevation causes arteriolosclerosis of

the kidney arterioles with secondary atrophy and fibrous replacement of the glomeruli giving rise to the typical granular kidney which eventually becomes contracted In less than 10 per cent of cases of hypertension does this atrophy of the kidney progress to the point where it gives rise to clinical symptoms of kidney insufficiency, with uremia or azotemia

Hereditary factors play an important role Because hypertension ordinarily becomes manifest at a relatively advanced age investigation of genetic factors is difficult but many studies have revealed a high familial incidence of hypertension among the brothers and sisters parents uncles aunts and grandparents of patients with hypertension In some families every member succumbs to one of the complications of hypertension on reaching the same age period usually at about 50

There is no direct relationship between arteriosclerosis and hypertension At least half of all patients with advanced arteriosclerosis never have hypertension and many hypertensives do not develop arteriosclerosis of the larger arteries As a rule however hypertensives do develop arteriosclerosis but the hypertension should be regarded not as the cause of the arteriosclerosis but as a factor that accelerates its development

Certain cases of hypertension are associated with endocrine disturbances The most striking are those associated with adrenal cortical tumors Hypertension is commonly encountered in patients with myxedema For many years clinicians have sought to relate hypertension in women to the menopause Hypertension in both men and women develops most often at the age when the menopause takes place so that the association may be merely accidental Young women with an artificial menopause due to operative removal of the ovaries or to radiotherapy do not exhibit hypertension More characteristic of the menopause than a permanent rise in pressure

is a marked lability of blood pressure This parallels the vasomotor disturbances of the flushes Hypertension is encountered more frequently in obese persons It is common in diabetics occurring in about one third of all those over 50

There has been growing interest in the so called psychosomatic aspects of hypertension and some have ventured the claim that hypertension is caused by personality disturbances and can be cured or relieved by psychotherapy Binger and his associates published a careful study of this matter[1] They found that hypertensives have neurotic personalities and have suffered from insecurity in their childhood and an unsatisfied dependent relationship to a threatening parent Binger believes that hypertensives differ from other persons with neurotic disorders in as much as they finally submit to the hostility of the parent figure and accept defeat of their own aggressive drives This leads to tenseness anxiety states and depressions They develop compensatory aggressive drives but remain insecure Anything that threatens their security increases their anxiety and depression Much of this anxiety is absorbed in their symptoms they rarely develop organized neurotic symptoms There is no proof that this type of personality disturbance is the cause of hypertension they are associated phenomena that have a common cause Moreover not every hypertensive need exhibit these character traits and not everyone who has such a personality disturbance has elevated blood pressure

Pathology —The characteristic lesion associated with hypertension is an arteriolosclerosis found chiefly in the arterioles of the kidneys spleen and pancreas Arteriosclerosis of the larger arteries is not constant Cardiac hypertrophy is found in almost every case in which the diastolic pressure is

[1] Binger C A L *et al* *Personality in Arterial Hypertension* (New York City American Association for Research in Psychosomatic Problems 1945)



Fig 8 — Extreme hypertrophy of the left ventricle in a patient with hypertension and hemiplegia



FIG 9 — Enlargement of the left ventricle and generalized dilatation of the aorta due to essential hypertension

persistent above 100 The left ventricle is first involved but right ventricular hypertrophy follows sooner or later These hearts may attain a tremendous size Coronary artery disease *may or may not be present Myocardial lesions depend on the state of the coronary arteries The kidneys may* be normal or they may show various degrees of arteriosclerosis with contraction Malignant sclerosis is uncommon in older persons Cerebral hemorrhage a common complication of hypertension is determined in many instances by the presence of miliary aneurysms of the cerebral arterioles These occur most frequently in the vessels of the corpus striatum and it is here that hemorrhage most often occurs

Symptoms

Significant hypertension is rare under the age of 40 commonest *between the ages of 45 and 70 and* less frequent again among the higher age groups for persons with hypertension usually die before they reach old age The condition is distinctly more common among women than among men

Often hypertension is discovered accidentally in the course of a routine physical examination of patients who are unaware of any deviation from normal health The elevation in pressure in such cases is usually not great maybe 175/95 There is no cardiac enlargement and no evidence of renal disturbance Measurement of the blood pressure of such a patient at different times of the day under varying conditions over a long period of years will demonstrate that it is undergoing constant and great fluctuations Early in the morning the pressure is apt to be low in the afternoon it is high Emotional upsets and mental strains are quickly reflected in a rise in pressure It is the systolic pressure in particular that is labile In these patients apparent cures are seen with par

ticular frequency under treatment or following an acute intercurrent infection the pressure at times returns to normal But the drop is only temporary In the course of weeks and months the pressure again rises and the former clinical picture is repeated In the early stages of the disease therefore the variability rather than the absolute height of the sphygmomanometric readings is of the greatest significance

This state of affairs may continue for five 10 or even 20 years without much change and few symptoms More often however there is a slow but steady tendency of the pressure to rise to higher levels With this it gradually becomes more stable the fluctuations are no longer so extreme and normal figures are rarely approached It is at this stage that the diastolic readings reach 105 and over and systolic readings 200 or more Now the patient has arrived at the stage of fully developed hypertension Hypertrophy and dilatation of the heart with possibly relative mitral insufficiency have become manifest and certain subjective complaints have appeared

Many patients first seek medical attention at this stage Among the earliest symptoms are headache vertigo and shortness of breath on exertion Nocturia is not infrequent although the kidney function is rarely impaired This nocturia is of cardiac origin from passive congestion of the kidney During the night s rest the circulation and with it the renal secretion improves The nocturia of Bright s disease is due to inability of the kidney to concentrate the urine so that large quantities of water must constantly be excreted to wash out the solids The two conditions may be differentiated by the fact that in nocturia of cardiac origin the specific gravity of the urine is high and in that of renal origin it is low In other cases repeated nosebleeds may give the first warning The bleeding comes from a small artery on the nasal septum which in most instances can be readily identified Epistaxis

in a person over 40 years of age should always suggest the possibility of an existing hypertension

Eyegrounds.—All patients with hypertension show changes in the eyegrounds The earliest and most constant sign is narrowing and increased tortuosity of the arteries The degree of narrowing roughly parallels the level of hypertension In more advanced cases particularly when there is rapid progress of the disease—the so called malignant hypertension—there are hemorrhages and white scars in the retina Papillitis is seen only in malignant sclerosis, and this is uncommon in older persons

For convenience of description the further symptomatology of essential hypertension is best discussed under several captions determined by the presenting symptoms The three chief forms of the disease may be termed the cardiac the cerebral and the renal

Cardiac form.—Symptoms referable to the heart dominate the clinical picture in over 50 per cent of cases The earliest sign is dyspnea on exertion This may at first be of slight degree The patient is apt to be plethoric, his face red or slightly cyanotic, the superficial veins in the neck and on the dorsum of the hand swollen Examination reveals a heart that is enlarged, especially to the left with the sounds of good quality and the aortic second sound accentuated A systolic murmur due to dilatation of the aorta is commonly heard at the aortic area Not infrequently an increased area of aortic dullness can be mapped out by percussion and demonstrated by the roentgen ray The pulsation of the aorta or innominate artery may be felt in the suprasternal notch and if the subclavian arteries share in the dilatation their pulsation may be visible above the clavicles The accentuation of the aortic second sound in these cases is due in part to the fact that the dilated aorta is longer than normal and being fixed at its root be-

comes more closely approximated to the anterior chest wall

The electrocardiogram shows left ventricular preponderance when the left ventricle has become enlarged In later stages of left ventricular hypertrophy the T waves in lead 1 or in leads 1 2 and 4 may become negative There may be a concomitant depression of the RT segments in these leads and the QRS complex may be widened to 0 11 or 0 12 second Such findings may be due solely to left ventricular strain and need not connote coronary artery disease

Sooner or later *cardiac insufficiency* becomes more marked and the systolic apical murmur of a relative mitral insufficiency becomes manifest Evidences of left ventricular failure dominate the clinical picture Dyspnea is the most striking symptom and is caused by engorgement of the pulmonary blood vessels At first shortness of breath appears only on exertion but soon it persists when the patient is at rest Congestive rales may appear in the lower lobes of the lungs In many cases nocturnal paroxysmal dyspnea becomes a distressing symptom which in its severest form is accompanied by pulmonary edema It does not differ from the similar condition observed in patients with coronary artery disease or with syphilitic aortitis for acute left ventricular failure is the cause of such paroxysmal dyspnea in all forms of heart disease *Gallop rhythm* heard at the apex is characteristic of the failing heart of hypertensives In the earlier stages of cardiac insufficiency it may appear only after exercise and so may become a valuable indicator of impending cardiac failure With gallop rhythm the heart rate is rapid and the pulmonic second sound is accentuated When the left ventricle fails the right ventricle too labors at a disadvantage and soon signs of right heart failure appear The neck veins become engorged the liver enlarges and ascites or edema of the legs may develop

In the vast majority of patients with hypertension the onset of severe myocardial insufficiency is accompanied by a fall of some 20 to 40 mm in the systolic pressure with no alteration or with a rise in the diastolic pressure When the myocardium weakens the systolic output of the ventricles diminishes and therefore the systolic pressure will be lowered but this does not affect the tonus of the peripheral arterioles which determines the diastolic pressure A small pulse pressure results which in hyperpiesis is pathognomonic for heart failure An arterial blood pressure reading of 160/120 or of 130/100 clearly signalizes the presence of serious myocardial weakness

The popular conception that the blood pressure in patients with hypertension drops to normal or subnormal figures when the heart fails is false This occurs only as a terminal phenomenon a few hours before death or with widespread infarction of the heart from closure of a main stem of the coronary arteries A marked drop in diastolic pressure is due not to cardiac failure but to a diminution or loss of the factor which determined the increased vascular tone

Alterations in cardiac rhythm are not uncommon The irregularity most frequently encountered is that due to extrasystoles They are rarely of much significance and do not affect the ultimate outcome of the case unless they are numerous and persistent Auricular fibrillation occurs in about 7 per cent of hospitalized cases but in far fewer ambulant patients The onset of auricular fibrillation is followed by the usual evidences of heart failure which can be controlled by the proper administration of digitalis

Alternation of the pulse is common when the heart fails but it is rarely recognized because it is rarely sought for In few cases is it sufficiently marked to be capable of detection by the unaided finger In many it can be discovered by means

of the sphygmomanometer When the first arterial sound be comes audible as the air in the cuff is gradually released, the rate of the sounds will be exactly one half the heart rate for only every second beat is strong enough to come through at the systolic pressure As the pressure in the cuff is lowered 10 to 20 mm more all the pulse beats come through sud denly and the rate of the sounds is doubled Alternation is in most instances of grave significance The slower the pulse rate associated with alternation the graver the prognosis Coronary artery sclerosis in all of its manifestations is com monly associated with hypertension but the relationship between these two conditions is not causal or constant except that the hypertonia may contribute to the coronary artery disease In a certain number of cases an attack of substernal oppression may be the first symptom leading to the discovery of latent hypertonia Many hypertensives die of cardiac infarction

Cerebral symptoms —In a large number of cases the symp toms of hypertension are manifested by cerebral vascular dis turbances The earliest symptoms are those of a transient dis turbance of cerebral function Headaches sudden vertigo and confusional states which pass off rapidly are not un common Again there may be sudden aphasia or merely an impediment of speech which quickly disappears Other pa tients experience transient true hemiplegias A woman 52 years of age had known for seven years that her blood pres sure ranged about 180 One day she awoke vomited and found herself unable to talk or to move the right arm or leg Within about an hour speech as well as slight movements of the paralyzed limbs began to return and within about 12 hours all of the symptoms had disappeared with the excep tion of a severe headache Twenty years later although the moderate hypertension persisted there was no evidence of

any cerebral lesion nor had there been a repetition of the attack She finally died of a massive cerebral hemorrhage at the age of 77 Not infrequently an attack of hemiplegia is the first indication of the existence of hypertension Many of my hospital patients claim that they were well before their stroke The cerebral manifestations may take any of the forms described in the section on arteriosclerosis of the cerebral arteries

Renal symptoms —Symptoms due to disturbed kidney function are infrequent Only about 6 per cent of patients with essential hypertension succumb to uremia The presence of traces of albumin and casts in the urine is of little clinical significance The most important early sign of kidney insufficiency is inability of the patient to pass concentrated urine A simple concentration test will unmask this condition The patient is given no fluids after 6 00 P M The following morning he discards the first specimen of urine passed Specimens are then collected at 9 00 10 00 and 11 00 A M the patient in the meantime receiving no food or drink A normal kidney under such circumstances will secrete urine of a specific gravity of from 1 025 to 1 030 The degree of damage to the kidney is indicated by the specific gravity If the specific gravity does not exceed 1 015 there is considerable impairment of function but azotemia does not develop until the specific gravity becomes fixed at between 1 012 and 1 010 Azotemia is recognized by finding an increase in the urea nitrogen of the blood The normal figure is 15 mg per 100 cc of blood With kidney insufficiency the level of urea nitrogen rises gradually and may reach as high as 150 Severe cardiac insufficiency by causing passive congestion of the kidneys and thus interfering with their function may be accompanied by moderate retention of urea nitrogen Figures up to 40 or 50 mg per cent may be encountered This will clear up if cardiac compensation is restored

Prognosis

Patients do not die of hypertension as such but as the result of the damage to various organs particularly the heart arteries and kidneys caused by the prolonged excessive strain to which the cardiovascular apparatus is exposed Many years may elapse before such injury disturbs the normal mechanism of the body and the resistance of the several organs of different individuals to the insidious effect of the hypertensive state varies tremendously It is difficult therefore to generalize about the prognosis of hypertension

The younger the patient the worse the outlook Persons under 45 with marked hypertension rarely survive more than a few years Older individuals may survive five 10 or even 20 years in spite of persistently high blood pressure and symptoms pointing to beginning cardiac weakness or disturbance of the cerebral circulation Hypertension in persons over 70 is well borne and often gives rise to no complaints or symptoms The prognosis is much less favorable in men than in women

The diastolic blood pressure is of great significance in estimating the seriousness of the case A diastolic pressure which is persistently above 130 mm Hg is incompatible with survival for more than a few years and pressures that reach 150 predicate an early end Blood pressure readings taken from time to time in the physician s office may be very deceptive Emotionally tense patients may exhibit such high readings at every visit that the physician wonders how they survive I have patients who show pressures of 300/150 for years If one measures their blood pressure in their homes when they are relaxed one finds that the actual levels for most of the day are much lower

In patients with hypertension the causes of death in their

order of frequency are cardiac failure cerebral vascular insults coronary artery disease and uremia

To a certain extent the early symptoms complained of by the patient foretell the manner of his death Thus the majority of those in whom symptoms of myocardial weakness occur early die eventually from cardiac failure Those with angina pectoris are apt to die of cardiac infarction Headache suggests the probability of death from apoplexy or more rarely uremia

Clearly defined evidence of disturbed renal function such as fixation of the specific gravity of the urine and retention of urea in the blood provided it is not conditioned by cardiac failure is always of grave significance Death may be expected within a year

The majority of patients with hypertension however, survive many years particularly those whose disorder is discovered before the appearance of symptoms Their recuperative power after the onset of severe myocardial insufficiency is often so little short of marvelous that no patient should be given up as hopeless After an attack of apoplexy they may survive many years A good deal depends upon the mode of life of the individual If he can spare himself and remain under careful and prolonged medical supervision many years can be added to his existence even though he continues at his usual occupation

The earlier stages of hypertension are characterized by a purely functional disturbance an increased tonus of the arterioles which although anatomically normal are set so to speak in the position of partial contraction With this there is marked instability of the vegetative nervous system which leads to great and frequent changes in arteriolar tone with parallel variation in arterial blood pressure The early phases of arterial hypertension are marked particularly by instability

of the blood pressure and by disturbances in the domain of the involuntary nervous system It is only after many years that the secondary changes in the heart and arteries and in the kidneys occur

Management

The spontaneous wide variations in blood pressure have led to many false therapeutic claims Worry anxiety or excitement may lead to marked transient rises in blood pressure rest and relaxation will induce a drop If the patient is allowed to rest on a comfortable examining couch and blood pressure readings are made at short intervals the later readings will always be lower than the initial ones Not infrequently the systolic pressure may drop as much as 20 to 40 millimeters of mercury Just as the estimation of the metabolic rate is made with the patient under basal conditions so in taking comparative blood pressure readings the attempt should be made to obtain readings under circumstances that are as uniform as possible and that eliminate factors which may induce transient elevations in pressure Although in the daily practice of medicine it is rarely possible to obtain blood pressure readings with the patient in the fasting resting stage observations can be made with the patient relaxed and repeated readings can be made for five or 10 minutes until the blood pressure becomes more or less stabilized at a level which is ordinarily considerably lower than the initial one

It is this great variability of blood pressure and its tendency *to fall spontaneously that makes difficult the evaluation* of different forms of therapy and that has led to so many fads in the treatment of arterial hypertension Innumerable drugs have been exploited with enthusiasm for a few months or years only to be discarded and forgotten

Prevention —Arterial hypertension cannot be prevented so long as we are in complete ignorance of its cause It has repeatedly been claimed that the hurry and stress of our mode of living leads to arterial disease and hypertension and that it is responsible for the increasing mortality from these conditions Careful analyses have proved the incorrectness of this view so that the hope that arterial hypertension might be prevented by a return to the simple life is without foundation

Improper diet excessive use of alcohol and tobacco absorption of toxins from a sluggish colon and focal infections have severally been considered causative agents of arterial hypertension There is no evidence in support of these views Although high blood pressure is commonly encountered in obese individuals there is no direct connection between obesity and hypertension It seems more probable that some underlying constitutional disorder lies at the root of both conditions

It is becoming more and more apparent that hereditary factors are so important that arterial hypertension should be regarded as a familial disorder The discovery of a case of hypertension should call for periodic check up of other members of the family—brothers and sisters parents and children This will not prevent the development of the disorder but early recognition and appropriate treatment may help to minimize its ill effects and avoid or postpone the more serious complications Similarly periodic health examinations will reveal many instances of arterial hypertension in the asymptomatic stage and enable the subject to care for himself properly

Treatment —An individual who has no symptoms in whom elevation of blood pressure is accidentally discovered requires no active treatment He should be told that his blood pressure is a bit high but the physician should explain that as

a rule hypertension is well tolerated for years and that it calls for the avoidance of excesses of all kinds and the establishment of sensible habits of living The exact level of blood pressure should not be revealed to the patient and the natural spontaneous variations in pressure should be made clear Many patients become slaves to the sphygmomanometer and are elated when the reading is 10 mm lower and become depressed and apprehensive when it is a few points higher than at a previous examination The blood pressure should not be measured too frequently

The earliest symptoms of hypertension are headache vertigo flushes sticking precordial pain and palpitation These symptoms are related to the disturbance of the vegetative nervous system and do not as a rule reflect organic disease

In the early stages of the disorder treatment should concern itself with regulation of the patient s life and with allaying his fears The patient should discipline himself to moderation in every bodily and mental activity temperance in eating drinking smoking exercise work and pleasure If he can learn to slow the tempo of his living and go through his daily routine without undue fuss or hurry his capacity for work and accomplishment will remain large and his activities will actually be beneficial to him by maintaining his morale

With these precautions it is best for the patient to continue at his work In the case of the business executive the professional man or the clerical worker the occupation involves little physical strain Too great responsibilities leading to undue anxiety and worry should be avoided as far as possible The patient should learn to temper the drive of his ambition even at the cost of lessening his accomplishment Most factory hands employed at machines can carry on It is the heavy type of labor of the unskilled workman that is harmful

Whenever possible the patient should plan for at least two

vacations during the year The vacation should provide physical rest a change of scene and new interest Moderate exercise is beneficial Walking even long cross country hikes, offers the best form of physical activity Golf and horseback riding are permissible More violent sports such as tennis handball and baseball in fact all competitive games in which the participant drives himself to win are too strenuous Bathing and leisurely swimming may be allowed but should not be overdone The best check on the amount of exercise that can be borne without harm is the reaction of the patient himself Exercise should be followed by a sense of well being and should never be carried beyond the threshold of dyspnea and fatigue

Diet The diet should be liberal No particular food restriction will reduce the blood pressure or favorably influence the course of the disease It is still necessary to emphasize that protein is not harmful to persons with hypertension even when there is accompanying albuminuria Meat including red meat as well as eggs may be freely allowed indeed they are as essential to a well balanced diet here as in healthy persons Many patients with hypertension either on their own initiative or on the advice of their physician avoid all protein intake for months and years and in time suffer from protein starvation This may be so extreme as to lower the blood proteins and favor the occurrence of edema It is not uncommon to encounter moderate edema of the legs great weakness and some dyspnea in patients with arterial hypertension in whom careful investigation reveals no heart failure and no nephritis Such patients may be incorrectly treated for months with cardiac stimulants and diuretics and kept in bed but without improvement Inquiry will usually reveal protein starvation The administration of a high protein diet 100 to 125 Gm a day, and large doses of iron for there is usu

ally secondary anemia will lead to complete relief of symp toms within a few months Salt restriction which has been advocated by some is of no value in the absence of edema

Coffee and tea in moderation are not harmful if they do not provoke sleeplessness Strong alcoholic drinks and drink ing to excess are inadvisable because of the vasomotor reac tions which they induce A glass of wine or sherry often acts beneficially in promoting relaxation and allaying restlessness and irritability Smoking is permissible

In the presence of obesity the diet should be adjusted to in sure an adequate reduction in weight The total caloric intake is decreased by restricting the quantity of food and curtailing the fat and carbohydrate intake (see p 42) Eating is largely a matter of habit and if the patient is made to understand the importance of such an adjustment of diet he will soon learn to be content on the restricted regimen The first few weeks are difficult and are often marked by real hunger and weakness At times a few pieces of candy between meals or the administration of 2 5 to 5 mg of benzedrine sulfate tablets before meals tides the patient over the first weeks until he has become accustomed to the diet

The bowels should be regulated The administration of 3 gr of calomel at night followed by ½ oz of magnesium sulfate in the morning may relieve headache and vertigo This medication should not be repeated oftener than once every two to three weeks

Drugs No drugs will permanently lower the blood pres sure The nitrites even those with longer lasting effects such as erythrol tetranitrate induce only transient lowering of pressure and their by effects usually make the patient more uncomfortable Arterial dilators such as theobromine and metaphylline are also of little benefit as are the various muscle and pancreatic extracts Potassium thiocyanate tends

to reduce blood pressure and relieve the headaches and nervousness of hypertensive patients It is given in doses of from 5 to 15 gr a day so adjusted as to maintain a blood level not exceeding 10 mg per cent Some authors report favorable results but toxic reactions such as skin eruptions, weakness nausea and vomiting are common and over one half of the patients particularly those in the more advanced stages of the disease experience no benefit I have found little occasion to employ this drug

Maintenance of lower levels of pressure is best achieved by controlling the exaggerated nervous and emotional reactions of the patient Here sedatives are very useful The best of all is the classic mixture of chloral hydrate and sodium bromide The dosage should be adjusted to the individual from 5 to 10 gr of chloral hydrate and from 10 to 20 gr of sodium bromide in a vehicle such as aromatic elixir given two or three times a day The barbiturates too are very useful The usual dose is ½ gr of phenobarbital three times a day

In the early stages of essential hypertension it is not necessary or advisable to give treatment directed to the heart Some have advocated giving tonic doses of digitalis to strengthen cardiac contraction and to prevent heart failure but this is of questionable benefit Potassium iodide is of no value and does not prevent the development of arterial disease The administration of estrogenic hormone to hypertensive women with vasomotor disturbances of the menopause may give symptomatic relief and control marked fluctuations of the blood pressure It does not permanently restore the blood pressure to normal Diethylstilbestrol may be given in a dosage of 0 5 mg daily, or else estradiol benzoate in oil 2 000 rat units by injection three times a week None of the other hormones are helpful

Any measure that promotes muscular and mental relaxa

tion tends to lower the blood pressure Warm baths at a temperature of about 100 F are often very soothing These are best taken before retiring at night or before an afternoon siesta Electrotherapy may have a similar effect Some have had success with exercises planned to induce muscular relaxation [2] Occasional one or two week periods of bed rest are probably more valuable than all of the other measures combined But care should be taken so to plan these enforced vacations that the benefit from the body rest is not counteracted by worry and irritation at the inactivity

Surgery In recent years a number of operations to lower blood pressure have been devised The rare cases of paroxysmal hypertension due to suprarenal tumors can be cured by operative removal of the tumor [3] Peet[4] has devised a technic of bilateral supradiaphragmatic splanchnicectomy with lower dorsal ganglionectomy He claims that one of every three patients with malignant hypertension who are operated on survives five years or longer and that many others experience reduction in blood pressure and symptomatic improvement White and Smithwick[5] report less favorable results with this procedure and Smithwick now uses a combined supra and infradiaphragmatic approach with removal of the sympathetic trunk from the tenth dorsal to the third lumbar with excision of the great splanchnic nerves The operative mortality is small This operation produces marked postural hypotension which gradually disappears in the course of a

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Maloney W J and Sorapure V E Relief of High Vascular Muscular and Mental Tension New York M J 99 10_1 1914

[3] Coller F A Field H Jr and Durant T M Chromaffin Cell Tumor Causing Paroxysmal Hypertension Relieved by Operation" Arch Surg 28 1136 June 1934

[4] Peet M M Wood W W and Braden S 'The Surgical Treatment of Hypertension" J A M A 115 1875 Nov 30 1940

[5] White J C and Smithwick R *The Autonomic Nervous System* (2d ed New York City The Macmillan Company 1941)

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[2] Maloney W J and Sorapure V E Relief of High Vascular Muscular and Mental Tension New York M J 99 1021 1914

[3] Coller F A Field H Jr and Durant T M Chromaffin Cell Tumor Causing Paroxysmal Hypertension Relieved by Operation Arch Surg 28 1136 June 1934

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few months Smithwick obtains favorable results in most cases in which the eyegrounds do not show advanced changes and in which preoperative testing with large doses of sodium amytal induces a fall of blood pressure to normal Reduced renal or cardiac function and cerebral vascular damage in general are contraindications to operation for in such cases the results are poor Most patients over the age of 50 do not respond favorably and are poor operative risks Although undoubtedly brilliant results have been achieved in individual cases the ultimate value of these operations is still an open question Many years will elapse before one can judge whether they prolong the lives of hypertensives for the course of hypertension is a long one The patients who respond best to operation in general are those with the best outlook under a medical regimen For the present I should be inclined to restrict operation to young individuals with progressive severe hypertension but with good kidney function

Complications—There are a number of symptoms that are particularly troublesome to both the patient and the physician Chief among these is headache which should be treated by the general measures that have been described Caffeine or aminophylline often relieves hypertensive headache If these are ineffectual and particularly if the blood pressure is rising or is at a very high level and if bed rest brings no relief a phlebotomy of about 500 cc should be done This often abolishes the headache immediately and remarkably enough the respite may last for several months Blood letting in such cases not alone ameliorates symptoms but may prevent the occurrence of a cerebrovascular accident Severe persistent headache with a mounting diastolic pressure always calls for active treatment for it is often a warning of impending apoplexy

Tinnitus aurium may be very disturbing One can only

employ the general measures that have been outlined but often they are ineffectual Vertigo may at times be relieved by wearing a well fitting corset or abdominal binder that pulls in the lower abdomen

Kidney insufficiency is a relatively unusual complication of essential arterial hypertension When true uremia sets in treatment is of little avail More often oliguria and slight azotemia result from heart failure and may recede as a result of supportive measures directed to the heart

Heart failure may be due to gradual flagging of an over taxed myocardium or to complicating disease of the coronary arteries Its treatment does not differ from that of heart failure due to other causes

Chapter Seven

DISEASES OF THE CARDIOVASCULAR SYSTEM—SYPHILIS

SYPHILIS is the cause of about 10 per cent of heart disease in persons past the age of 50 Syphilis of the myocardium is rare the common lesion is in the aorta Routine examination discloses that about 10 per cent of individuals with late syphilis have syphilitic involvement of the cardiovascular system More intensive study with roentgen rays reveals an incidence of some 33 per cent and autopsy studies indicate a still greater frequency of aortic involvement in males with late syphilis These data point to the necessity of searching for cardiovascular syphilis in every known syphilitic and in view of the late appearance of signs of cardiovascular syphilis—on the average 20 years after the initial infection—of repeating examination annually Cardiovascular syphilis is often associated with cerebrospinal syphilis and tabes and paresis

The frequency of syphilis in any group of individuals depends on the classes of society from which they are recruited In the male wards of a city hospital positive Wassermann reactions may run as high as 25 per cent On the other hand among applicants for license to peddle in New York City who were subjected to routine Wassermann tests 8 4 per cent were found positive

Syphilitic disease of the aorta is four to five times as common in men as in women and twice as common in Negro as in white patients

The symptoms of syphilitic aortitis appear in the majority of patients between the ages of 45 and 50 Acquired syphilitic aortic disease may occur as early as age 25 or as late as age 70 The period elapsing between the contraction of the chancre and the development of symptoms of aortitis is on the average 20 years At what time actual infection of the aorta occurs is unknown but it must antedate by many years the onset of typical symptoms The shortest period between the primary infection and death from syphilis of the aorta is one year the longest 55 years I have a patient who had a chancre at age 20 and who first developed syphilitic aortitis at age 58

Syphilitic aortitis is localized most commonly in the ascending aorta particularly in the suprasigmoid portion but it often involves the whole arch and not infrequently the entire thoracic aorta Syphilitic lesions of the abdominal aorta are rare As a rule the process stops sharply at the descending aorta or at the diaphragm

Pathology

The inflammation begins as a round cell infiltration around the vasa vasorum in the adventitia and media Gradually these areas enlarge and extend farther into the media With this the elastic and muscular layers of the aorta are destroyed and mononuclear, epithelioid and giant cells surround the necrotic areas These in fact constitute minute gummas Gradually this syphilitic granulation tissue invades larger and larger areas of the media and extends through to the intima In the course of time scarring takes place and with this the wall of the aorta becomes thinned and the

intima is drawn in and puckered over the scarred areas This pathological process produces a characteristic gross appearance of the involved aorta The aorta is usually dilated and the intima is wrinkled often with longitudinal striations

Atherosclerosis of the aorta is distinguished from syphilis by the fact that in the former the intima is primarily affected There is lipoid infiltration of the intima with secondary calcification ulceration and mural thrombosis The lesions are not confined to the thoracic aorta but extend down beyond the bifurcation into the iliac arteries Frequently the two lesions atherosclerosis and syphilis are combined and it may then be difficult to recognize the syphilitic lesions with the naked eye

In many instances the pathological process surrounds the mouths of the coronary arteries in the sinuses of Valsalva and may proceed to complete occlusion of the orifices Interference with the coronary blood supply results in infarction and scarring of the myocardium Syphilitic involvement of the coronary arteries themselves is very rare

The most common extension of the syphilitic process is to the aortic valves The lesion is quite characteristic The distortion of the wall of the aorta at the insertion of the valves leads to a widening of the commissures between the valve leaflets As a result the free margins droop and become everted and in the course of time they become thickened or rolled This leads to insufficiency of the aortic valves

Aneurysms of the aorta with few exceptions develop on the basis of a syphilitic aortitis From 80 to 90 per cent of aneurysms of the thoracic aorta are syphilitic in origin Their location corresponds to the site of predilection of syphilitic infection of the aorta Boyd,[1] in an analysis of 4 000 aneurysms

[1] Boyd L. J "Study of 4 000 Reported Cases of Aneurysm of the Thoracic Aorta" Am J M Sc. 168 654 November 1924

found the ascending aorta the arch the descending and thoracic aorta involved in the ratio of 10 7 3 1 In very old individuals extensive atherosclerosis may cause aneurysms These are often multiple and most commonly arise from the abdominal aorta although rarely they may be thoracic The average age at death in 20 cases collected by Ruffin was 72 7 years One third of the patients died of rupture of the aneurysm Other rare causes of aneurysms are rheumatic fever tuberculosis of the aorta and trauma We shall confine our description to syphilitic aneurysms

An aneurysm is a localized dilatation of the arterial wall It may be diffuse and fusiform from 6 to 10 cm long or more commonly it may be saccular Aneurysms arise as a result of the injury to the elastic and muscular tissue of the media by the syphilitic process The wall of the aorta gives way in the weakened areas but the wall of the aneurysmal sac is not simply the dilated aortic wall If one traces the several layers of the aortic wall from the healthy aorta into the sac one finds that the intima and media stop abruptly at the entrance to the aneurysm The wall of the sac is made up of newly formed white and elastic connective tissue into which have been fused not alone the adventitia but any other structures with which the aneurysm comes in contact during its growth Thus veins the mediastinal fascia and even bronchi may be incorporated into the wall of the sac

The inner surface of the sac tends to be covered with endothelium but often is thickened and calcified Thrombi commonly form within the sac and these as a rule become laminated and organized thus serving to strengthen the wall

As the aneurysm grows it impinges on the mediastinal structures that surround it and causes secondary changes in them Thus the vertebrae ribs or sternum may be eroded the bronchi may be compressed with secondary bronchiec

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FIG. 11—Arteriosclerosis of the aorta. Note crescentic shadow at the aortic knob representing a cross section of a calcified plaque.



Fig 12.—Syphilitic aortitis *left* roentgenogram fusiform dilatation of the aorta *right* pathologic specimen of the same case

tasis the recurrent laryngeal nerve is often destroyed and the esophagus may be displaced and partially occluded

Rupture of the aneurysmal sac causes death in about one half of the cases This occurs most frequently into the pericardium pleura or lung pulmonary artery or superior vena cava The aneurysm may rupture externally

The heart itself as has been pointed out rarely shows any direct syphilitic involvement In uncomplicated aortitis or in aneurysm the heart is normal Indeed it is often striking to see a small heart that looks almost like an appendage to a huge aneurysm When the coronary arteries are occluded the usual phenomena of cardiac infarction occur With aortic insufficiency dilatation and hypertrophy of the left ventricle take place and are often marked In the later stages the other chambers of the heart also undergo enlargement

Symptomatology

The clinical manifestations of syphilitic aortitis are best discussed in several categories determined by the presence of certain complications simple uncomplicated aortitis aortitis with aortic insufficiency aortitis with involvement of the mouths of the coronary arteries and aortitis with aneurysm of the aorta

Simple aortitis —In the absence of one of the complications just enumerated syphilitic inflammation of the aorta gives rise to no symptoms Fully one quarter of cases discovered at autopsy are unsuspected during the patient s life Much has been written concerning aortic pain so called aortalgia and attempts have been made to distinguish this particular type of pain from other forms of cardiac pain It has been described as a continuous pressing pain behind the manubrium There is no valid evidence for these views for pain does not



Fig 13 —Syphilitic aortitis saccular aneurysm of the aorta

occur in simple syphilitic aortitis Paroxysmal dyspnea too does not torment the patient with uncomplicated aortitis but is experienced only if there is an accompanying insufficiency of the aortic valves hypertension or aneurysm

The diagnosis must be based on the history the physical signs and the roentgen examination Because of this most cases are missed until some complication has supervened The discovery of simple syphilitic aortitis is usually accidental or else the result of a careful examination of a known syphilitic This is very unfortunate for the only hope of successful therapy lies in early diagnosis and treatment It is therefore exceedingly important to subject persons infected with syphilis to periodic examinations in order to discover any lesion in its earliest stages

The physical signs are those of aortic dilatation and elongation and do not differ from those characterizing atherosclerotic or other forms of aortic disease Even when the physical signs are definite the diagnosis in the last analysis depends on the known presence of syphilis as revealed by the Wassermann reaction or other data as well as on the age of the patient

Syphilitic aortitis involves chiefly the ascending portion of the arch and results in dilatation and elongation of the vessel It is the elongation more than the dilatation that gives rise to physical signs The aorta approaches closer to the anterior chest wall and extends to the right of the sternum It also ascends in the thorax so that its pulsation may be felt by inserting the finger in the suprasternal notch In its ascent it carries with it the origin of the innominate artery so that the right subclavian rises and its pulsation can often be felt above the clavicle It is only in rather extreme dilatation that the aorta extends to the left of the sternum

On palpation one may note pulsation in the second inter

space to the right of the sternum as well as the diastolic shock accompanying the closure of the aortic valves As Hoover pointed out the muscular sense of the muscles which lead from the head to the neck and shoulders is much more delicate than that of the thoracoscapular muscles so that an expansile pulsation can best be appreciated by placing the ear over the second right intercostal space The diastolic shock can best be felt with the distal ends of the metacarpal bones

Percussion reveals dullness in the second intercostal space to the right of the sternum Accentuation of the second aortic sound is due not to an alteration of intra aortic pressure or a change in the structure of the valves but to the close approximation of the aorta to the chest wall In the absence of aortic disease it occurs when the aorta is pulled to the right by fibroid disease of the right upper lobe of the lung Aside from accentuation the second aortic sound may undergo a change in quality and become tympanitic This tympanitic aortic second sound is indicative of disease of the aortic ring the root of the aorta and possibly of the valves It has nothing to do with accentuation and the occurrence of the two phenomena is quite distinct Thus there may be accentuation alone or a tympanitic quality alone or the two may be combined depending on the local lesion When present the tympanitic second aortic sound the *bruit de tabourka* of the French is of distinct diagnostic value A systolic murmur in the second interspace to the right of the sternum always accompanies dilatation of the ascending aorta It is produced by eddies in the blood stream as the blood passes from a vessel of smaller to one of larger lumen in this case as it passes through the normal aortic orifice into the dilated ascending aorta

Roentgenoscopic examination is a valuable supplement to physical examination Fluoroscopy yields more information than does the film Roentgenoscopy will reveal only dilata

tion and increased density of the aortic shadow and these changes are common to aortic dilatation from various causes —atherosclerosis hypertension aortic insufficiency and syphilis The information yielded by roentgen examination will rarely by itself allow of a positive diagnosis of syphilitic aortitis It must be evaluated in connection with the other clinical data

Dilatation of the ascending aorta in the anteroposterior view is manifested by an extension of the aortic shadow to the right of the sternum just above the arc formed by the right auricle The aortic knob is more prominent on the left The transverse diameter of the aortic shadow may be increased Measurements of the width of the aortic shadow are of little value When dilatation is extreme measurements are unnecessary when it is slight their interpretation is equivocal In the right oblique position dilatation of the ascending aorta may be visible In the left oblique position in which the course of the whole arch is often visualized the dilated first portion of the arch often stands out clearly on the left arising just above or even within the shadow of the right auricle Dilatation of the transverse and descending aorta is also readily demonstrable An increased density of the aortic shadow may be apparent This is due to the increased volume of the aorta filled with blood that must be penetrated by the roentgen rays and also to actual thickening of the aortic wall Occasionally a sharply localized dilatation of the root of the aorta is seen Such a finding is most characteristic of syphilitic aortitis The other changes are found in other forms of aortic dilatation as well

The diagnosis of syphilitic aortitis rests on the demonstration of the presence of dilatation of the aortic arch in a patient who is a known syphilitic If there is accompanying hypertension or if the patient is over 60 years old it is im

possible to ascertain whether the dilatation is caused by a syphilitic lesion or by an atherosclerotic or simple dilatation The younger the patient in the absence of complicating lesions the greater the probability that the dilatation is due to syphilis A history of syphilis a positive Wassermann reaction which occurs in about 75 per cent of cases or the finding of other stigmata of syphilis especially of cerebro spinal syphilis are as important as the demonstration of the presence of aortic dilatation

Aortic insufficiency—This is the most common complication of syphilitic aortitis and is found in over one third of the cases It is usually a late manifestation of syphilitic infection of the aorta and when discovered presages a relatively early death Unfortunately symptoms sufficient to lead the patient to consult his physician rarely arise until this or some other complication equally serious has set in

The commonest complaint is dyspnea which is found as the presenting symptom in three quarters of the cases It may take the form of ordinary dyspnea such as is seen in sufferers from heart disease appearing first after exertion and then gradually as compensation lessens becoming continuous, or it may be paroxysmal Dyspnea of either type is rather sudden in its onset

Paroxysmal dyspnea is a dramatic and terrifying phenomenon The attacks come suddenly with little or no warning and usually at night after the first or second hour of sleep The patient awakens with intense air hunger and fear of suffocation He may dash to the window to get more air or may evince marked motor restlessness in bed But in a few moments all of his efforts are directed to the act of breathing for a typical asthmatic seizure of the severest sort has set in He sits still bracing his hands for additional support and brings into use all of the accessory muscles of respiration

Just as in true asthma the dyspnea is ordinarily expiratory The chest becomes hyperresonant and squeaking rales and tracheal rhonchi become audible The patient becomes pale and breaks into a cold sweat As the attack continues some cyanosis becomes evident in the face and extremities Pain may or may not accompany the attack it is not an essential feature When it occurs it cannot be distinguished from the pain of angina pectoris Quite constant even in the absence of pain are tremendous anxiety and fear of impending death The pulse is rapid and the blood pressure usually greatly increased I have not uncommonly seen figures of from 225 to 300 mm Hg systolic There may be involuntary urination and defecation The attack usually lasts from five to 30 minutes and subsides almost as suddenly as it begins Toward the end of the attack the patient may cough up some blood stained mucus Pulmonary edema is not characteristic of these attacks but may supervene toward the end of prolonged severe seizures After the attack the breathing pulse rate and blood pressure return to their original figures and the patient completely exhausted sinks back on his pillows and often falls asleep

The cause and nature of cardiac asthma or paroxysmal dyspnea have been much discussed during the past one hundred years but we are still far from a complete answer Hope[2] writing in 1832 was the first clearly to distinguish the form of paroxysmal dyspnea that we have been discussing and to point out that it occurred particularly with hypertrophy and dilatation of the heart and aortic disease that it was associated with little expectoration and that its incidence was chiefly nocturnal It was Traube[3] who established the

[2] Hope James A *Treatise on the Diseases of the Heart and Great Vessels* (London 1832) p 345

[3] Traube L Bemerkungen uber das Asthma cardiale" *Gesammelte Schriften* (Berlin 1878) Vol III

teaching which still prevails that the asthmatic attack is caused by sudden failure of the left ventricle with resultant acute congestion of the lungs

Much of the lack of clarity that prevails is due to a confusion of different forms of severe dyspnea The dyspnea seen in mitral disease with acute edema of the lungs and signs of general venous stasis is quite different from the paroxysmal form occurring in aortic disease In the latter all of the classic signs of congestive heart failure are absent The paroxysmal dyspnea accompanying coronary disease while resembling much more closely the form of cardiac asthma that we are discussing differs in that signs of congestive heart failure quickly supervene and the blood pressure falls An explanation of the paroxysmal dyspnea that is so characteristic in certain cases of marked left ventricular enlargement is by no means simple Certainly some reflex mechanisms must be intimately concerned with the genesis of these attacks for they come and go too suddenly to be explained solely on the basis of acute failure of the left ventricle

Wassermann[4] endeavored to reconcile all of these conflicting elements into a theory of cardiac asthma The typical attack occurring during sleep is favored in its development by the physiological changes that accompany sleep There is a preponderant vagus action the heart slows there is lessened oxygen consumption with superficial respiration and a poorer aeration of the lungs Many reflexes are abolished and the threshold of response of the medullary centers is raised Thus considerable anoxemia may develop before the usual compensatory adjustments are made Suddenly when it reaches a certain degree all of the reflex mechanisms of defense seem to be activated and many of the medullary centers respond

[4] Wassermann S *Neue klinische Gesichtspunkte zur Lehre vom Asthma cardiale* (Berlin Urban & Schwarzenberg 1926)

There appear the sudden violent respiratory movements the bronchi are constricted through vagus action the blood pressure is elevated the pulse rate accelerated the skin vessels constricted There may be involuntary urination or defecation The drug that gives greatest relief is not a cardiac stimulant but a depressant of the nervous system—morphine As the attack continues the increased blood flow the excessive inspiratory suction on the blood in the large veins together with the relative mitral insufficiency that is usually present cause an overfilling of the pulmonary veins which may result in pulmonary edema An analogous mechanism prevails in the diurnal attacks but here the part played by failure of the left ventricle is greater so that the added depressing effect of sleep is not essential to initiate an attack From this it follows that diurnal attacks offer a graver prognosis than do nocturnal ones

The appearance of paroxysmal dyspnea in a patient with syphilitic aortitis is always of serious import It betokens a precarious state of the circulation Patients may continue for months with these attacks and with a fair degree of comfort between paroxysms but usually congestive heart failure soon supervenes if death does not occur in the attack itself

Pain occurs as an early symptom in two thirds of the cases of syphilitic aortic insufficiency At times there is a constant dull pain under the upper portion of the sternum frequently aggravated by exertion More commonly the pain has the character of true angina pectoris It may occur during attacks of paroxysmal dyspnea or it may be associated with a rapid pulse rate and a rise in blood pressure The occurrence of pain in these patients almost invariably points to encroachment of the syphilitic process on the mouths of the coronary arteries in the sinuses of Valsalva These syndromes of pain therefore will be discussed in greater detail in the para

graphs on coronary disease as a complication of syphilitic aortitis Aortic insufficiency and the coronary syndrome are frequently associated

Syphilitic involvement of the aortic valves gives rise to the most classic picture of free aortic insufficiency There is no *need to enter into the full details of the symptomatology* and physical signs It is often impossible to differentiate syphilitic from other forms of aortic insufficiency by the physical signs alone Characteristically there are great enlargement of the left ventricle a loud gushing diastolic murmur to the left of the sternum or at the apex and a marked Corrigan pulse with all of the peripheral vascular signs The pulse tracing of the subclavian artery has a sharp peak and never shows the anacrotic changes or the broadening of the peak often seen in rheumatic or atherosclerotic aortic insufficiency The reason for this is that aortic stenosis even of mild degree which is so common in the latter two conditions is never encountered in syphilitic aortic insufficiency

Hypertension with elevation of both systolic and diastolic pressures occurs in about 15 per cent of the cases I have seen figures as high as 260 mm Hg systolic and 120 diastolic In *such cases granular kidneys are found at autopsy The hyper*tension adds to the load on the left ventricle hastens onset of heart failure and favors the occurrence of paroxysmal *dyspnea*

Fever is a not uncommon feature of syphilitic aortitis and may provoke suspicion of an active rheumatic or bacterial *infection The differentiation may be difficult particularly in* view of the fact that moderate splenic enlargement is found in many patients with syphilitic aortitis

Subacute bacterial endocarditis may arise from the engrafting of Streptococcus viridans on the syphilitic lesions It is apt to take a rather virulent form and lead to early death

It can be recognized by the many embolic phenomena petechiae red blood cells in the urine infarcts of the spleen, kidneys or brain and by blood culture Recognition of this complication in a patient with known syphilitic aortitis offers no difficulties It is more difficult when one sees for the first time a patient with manifest subacute bacterial endocarditis and an aortic lesion to determine whether syphilitic aortic insufficiency forms the original basis of the infection A careful survey of all of the etiological and clinical features of the case will usually lead to the correct diagnosis

Once syphilitic aortic insufficiency has become clinically manifest the progress of the disease is as a rule rapid In general the more recent the syphilitic infection before the onset of cardiac symptoms the more rapid the development of cardiac failure The cases associated with tabes dorsalis are frequently indolent and asymptomatic and may go on for years Indeed in them the lesion is often discovered accidentally in the course of a routine examination The average time between the onset of symptoms of syphilitic aortic insufficiency and death is given as about one year This figure is based on hospital experience It seems probable that in patients seen in private practice who can take better care of themselves the average duration of life is much longer The progress of the disease is marked by the development of signs of congestive heart failure All of the chambers of the heart become greatly enlarged and the heart becomes progressively more and more insufficient Congestion of the lungs and liver and peripheral edema set in At this stage the heart does not respond to cardiac stimulants Auricular fibrillation however rarely develops This feature is important in differentiating syphilitic from other forms of aortic disease The presence of auricular fibrillation even when the Wassermann reaction is positive should arouse suspicion of another etiological factor

Psychoses are common in the later stages of decompensation As Head has pointed out they occur more frequently in aortic disease than in any other form of cardiac defect but they are not related to syphilitic affection of the brain Hallucinations of vision and of hearing and a sense of anxiety appear These are followed by paranoid delusions which may cause great motor excitement and restlessness The appearance of a psychosis usually indicates an early lethal outcome

Death results from progressive heart failure in about half of the cases of syphilitic aortic insufficiency Sudden unexpected death is another common mode of termination and is peculiarly characteristic of this valvular lesion These sudden deaths are frequently due to coronary thrombosis but often at autopsy no anatomical cause of death may be ascertained One then predicates the onset of ventricular fibrillation Not a few of these patients die of some intercurrent disease or of some complication such as embolism

Diagnosis The recognition of the syphilitic origin of a given case of aortic insufficiency is not always simple The first and most important criterion is the establishment of the fact that the aortic valve is the only one diseased for syphilis in contradistinction to rheumatic and atherosclerotic processes attacks none of the other valves of the heart A history of syphilis and the absence of past rheumatic infection are important The age of the patient is a valuable guide Aortic insufficiency in individuals below the age of 30 is usually rheumatic in those between the ages of 30 and 60 it is frequently syphilitic in those over 60 it is usually atherosclerotic in origin This rough rule applies in latitudes in which rheumatic fever is prevalent Farther south where rheumatic infection is rare relatively more cases of aortic insufficiency are of syphilitic origin A positive Wassermann reaction assists in the diagnosis but from 10 to 20 per cent of persons with

syphilitic aortic insufficiency give negative reactions and positive reactions are not uncommon in individuals with heart disease and with syphilis which has not localized in the aorta Syphilitic involvement of the central nervous system or of some other organ in the body may determine the diagnosis Still more helpful is the presence of an aneurysm of the aorta Aortic dilatation alone can rarely be used as a differential feature for in both rheumatic and atherosclerotic aortic insufficiency dilatation of considerable degree is common Paroxysmal dyspnea and anginal pain while not pathognomonic occur much more frequently in the syphilitic forms of this valvular defect Syphilitic aortic insufficiency never leads to aortic stenosis so that the presence of any signs pointing to aortic stenosis excludes syphilis as an etiologic factor Similarly auricular fibrillation occurs so rarely in the syphilitic valvular defect that in its presence the diagnosis should be made with great caution

Coronary artery disease —The syphilitic process in the aorta frequently encroaches on the orifices of the coronary arteries in the sinuses of Valsalva although the arteries themselves are rarely involved This narrowing of the mouths of the coronary vessels restricts the flow of blood through them and gives rise to the syndrome of angina pectoris Such coronary involvement may occur in simple syphilitic aortitis but is more common when the process has also extended to the aortic valves

Pain occurring in patients with syphilitic aortitis is almost invariably due to narrowing of the coronary orifices The pain does not differ from that encountered in the ordinary forms of angina pectoris but is more often associated with marked vasomotor reactions and more commonly is situated under the manubrium than under the midsternum At first there may be just the usual substernal pain on effort with or

without radiation to the left shoulder and arm In the classic form of angina pectoris the patient is immobile during the attack and there is no change of pulse rate blood pressure or respiration In many patients with syphilitic aortitis the anginal attacks are characterized by flushing of the face, marked acceleration of the heart rise in blood pressure, increase in the respiratory rate and motor restlessness Such attacks are seen as well in certain patients with hypertension and with rheumatic aortic insufficiency It has been suggested that such attacks are caused not by coronary artery disease but by a reflex arising from the diseased aorta These attacks should be differentiated from the more usual anginal attack A number of such cases of angina have been described which at autopsy showed no disease of the coronary arteries either along their course or at their mouths Observations by Lewis support the view that in such attacks there is an actual spasm of the coronary arteries associated with a generalized vasoconstriction

The anginal attacks are often but by no means invariably associated with seizures of paroxysmal dyspnea

The diagnosis of coronary disease in patients with syphilitic aortitis is always suggested by the occurrence of angina pectoris Further evidence may be found by electrocardiographic examination Abnormalities in the T wave are the most frequent finding Juster and Pardee from a study of autopsy material found that such abnormal T waves are due to encroachment on the lumen of the coronary orifices by the syphilitic disease in the sinuses of Valsalva Such electrocardiographic changes were found in 85 per cent of patients with syphilitic aortic insufficiency and in only 38 per cent of those with uncomplicated syphilitic aortitis The T wave may show the typical "coronary form

The prognosis is always grave in patients with syphilitic

aortic insufficiency and angina pectoris Sudden death is common

Treatment

The only hope of curing syphilitic aortitis lies in treating the patient in the earliest stages of the disease while the pathological process is still confined to the aorta proper But even with more advanced lesions treatment intelligently carried out often leads to prolongation of life and relief from symptoms Carelessly given it may hasten death or increase invalidity

A danger of antisyphilitic therapy lies in the Herxheimer reaction a transient inflammatory response in the local lesion of the heart or aorta which may lead to sudden death or acute congestive heart failure Rapid scarring of a gummatous lesion may induce rapid increase of the anatomical deformity in the heart Sudden death may follow directly on the administration of arsphenamine due presumably to ventricular fibrillation Many cases are on record of patients who had never had congestive heart failure who developed dyspnea orthopnea congested liver and edema directly following injudicious specific therapy Again an aortic aneurysm may rupture within 24 hours of an injection More rarely pre existing murmurs may become harsher or a fresh aortic diastolic murmur may develop during the course of treatment In these cases the scar accompanying healing increases the deformity of the valve

A growing appreciation of the complications that may follow antisyphilitic therapy with a more hopeful outlook in regard to the results that may be achieved has led in recent years to a safer conservative plan of treatment which in expert hands has given good results

Certain patients with syphilitic aortitis are best left un

treated These are patients without symptoms usually individuals 65 years or older often with neurosyphilis as well in whom the cardiovascular lesion has been discovered accidentally In them the prognosis even if they are left alone is fair and treatment may in some way disturb the balance between the activity of the spirochetes and the resistance of the body and lead to rapid progress of the lesion The Wassermann reaction of the blood is no guide to treatment Moreover as Moore has pointed out clinical and pathological progress of the lesion may occur in the presence of a negative Wassermann reaction of the blood

In all cases specific treatment should be delayed until signs of circulatory failure and the subjective symptoms of pain or paroxysmal dyspnea have been largely relieved by general medical treatment This includes bed rest limitation of fluids and salt and the administration of digitalis and diuretics

When the symptoms of cardiac failure have been controlled antisyphilitic therapy may be carefully instituted It is best to begin with the intramuscular injection of bismuth in oil 0 1 Gm every four to five days If this is well tolerated the dose is increased to 0 2 Gm after five injections and this is given once a week Potassium or sodium iodide is given by mouth at the same time as the bismuth in a dosage of 1 Gm three times a day increasing rapidly to 4 Gm three times a day This treatment with bismuth and iodides is continued for 12 weeks If the patient has not recovered a satisfactory cardiac reserve no arsenical is given but the same course of treatment is repeated after a rest period of about two months If there is no cardiac embarrassment the bismuth injection is followed by a course of neoarsphenamine Arsphenamine itself should not be used for it more readily produces untoward reactions The initial dose of neoarsphenamine is

0 1 Gm and this is cautiously increased at weekly intervals until a maximum dosage of from 0 3 to 0 4 Gm is reached Twelve injections are given Then the course of bismuth and iodides is resumed to be followed again by neoarsphenamine Mapharsen is less toxic than neoarsphenamine and may be used in its place The initial dose is 0 02 Gm It should be gradually increased to a maximum of 0 04 Gm Ideally, treatment should be continuous for at least two years and even after this period has elapsed it should be continued at intervals as long as the patient lives Mercury injections may be substituted for bismuth if desired

Penicillin will probably displace the arsenicals in the near future but the effective dosage and course of treatment have not yet been worked out Adequate treatment probably requires 80 000 units every three hours day and night for 7½ days This should be preceded by a course of bismuth

Untreated patients with syphilis of the aorta die on the average in 12 to 24 months after the onset of symptoms Moore in an exhaustive study of 169 patients showed that in well treated patients the average duration of life can be extended to about six years Many of these patients are relieved of pain and dyspnea remain free from cardiac symptoms and resume work

The treatment of paroxysmal dyspnea and of angina pectoris due to syphilitic aortitis is the same as that outlined for patients in whom these syndromes result from coronary artery disease

In patients in whom severe anginal seizures persist in spite of all therapy paravertebral nerve block with alcohol is very useful and often gives complete relief The same procedure may be used in patients in whom pressure or erosion of a large aneurysm causes much pain The ganglia to be injected are determined by the distribution of the pain

In rare cases of saccular aortic aneurysms the attempt may be made to cause a clot to form in the aneurysmal sac by inserting many yards of fine wire into the sac and passing a galvanic current through the wire This method or one of its variations has been employed with varying success by many surgeons[5] It can be used only in saccular aneurysms with a small communication with the aorta At best this treatment results in complete closure and fibrosis of the aneurysmal sac but failures are more frequent than successes and complications such as embolism hemorrhage or infection are not uncommon The many other methods that have been employed to obliterate the aneurysmal sac are still less successful

[5] Finney J M T "Wiring of Otherwise Inoperable Aneurysms" Am. J Surg 55 661 1912.

Chapter Eight

DISEASES OF THE CARDIOVASCULAR SYSTEM— VALVULAR DISEASE AND IRREGULARITIES

ALTHOUGH coronary artery disease and hypertension are responsible for the majority of cases of heart disease in per sons past the age of 50 valvular heart disease is by no means uncommon Syphilitic heart disease which leads to aortic in sufficiency has been discussed in Chapter 7 It accounts for about 10 per cent of all cases of heart disease in adults but a somewhat lower percentage in the older age periods

Although rheumatic fever and rheumatic valvular disease are preeminently conditions encountered in the young many cases are seen in older persons As a rule rheumatic fever with consequent damage to the heart valves attacks persons under the age of 20 The majority of these die of rheumatic reinfection or of the mechanical effects of their valvular de fects before they reach their fortieth year Some 10 per cent of those who contract rheumatic heart disease in their youth survive to the age of 50 These are persons who have had a relatively mild infection with few or no recurrences and with little mechanical handicap to the heart Among older persons with rheumatic valvular disease there are also those who contracted their initial rheumatic infection at a more ad vanced age—in the fourth or fifth decade Rarely the initial

rheumatic infection occurs after the age of 50 Rheumatic valvular disease occurs but is unusual after the age of 60 In most of these cases the valvular deformity and the resulting mechanical handicap to the heart are not extreme and the lesion is nonprogressive or very slowly progressive so that significant symptoms do not develop for many years Often in later life an atherosclerotic process with calcification is superimposed on the valve scarred by the ancient rheumatic infection and it is this secondary atherosclerosis that by further damaging the valve leads to heart failure Even in elderly persons rheumatic reinfection occurs and many instances of heart failure in older persons with rheumatic valvular disease are due to acute or subacute rheumatic carditis Rheumatic valvular disease may affect the mitral or aortic valves or both In the aged tricuspid disease is unusual With mitral disease auricular fibrillation is common

Arteriosclerotic valvular disease occurs after the age of 60 It involves the aortic valve more often than the mitral

Mitral Stenosis

Mitral stenosis is not uncommon between the ages of 50 and 60 About 20 per cent of all cases of mitral stenosis are encountered in persons past the age of 50 Most of these are rheumatic in origin and in some the lesion dates to a solitary mild rheumatic infection in childhood I saw a man of 64 whose mitral lesion was due to a solitary attack of polyarthritis at the age of 7 After the age of 60 one encounters occasional cases of arteriosclerotic mitral stenosis The lesion in these cases is a nodular calcification of the fibrous auriculoventricular ring which narrows the auriculoventricular orifice but to a less degree than does the typical endocarditic form of mitral stenosis The mitral leaflets are thickened and

sclerotic but not fused The calcified ring may be visualized by fluoroscopic study of the heart if the observer is well accommodated The consequences of mitral stenosis in elderly persons are identical with those in the young First there is enlargement of the left auricle and right ventricle followed later by left ventricular enlargement Eventually heart failure results Auricular fibrillation is a common complication Hypertension occurs in fully one half of all persons with mitral stenosis past the age of 50 The cause for this association is not clear Embolism to the cerebral renal or peripheral arteries is common The embolus arises from a thrombus in the left auricle

AORTIC INSUFFICIENCY

Aortic insufficiency when it is associated with mitral stenosis is due to rheumatic infection Solitary aortic insufficiency in older persons may be due to syphilis to arteriosclerosis or to a functional dilatation of the aortic ring This last condition arises only with marked hypertension or with grave anemia After the age of 60 arteriosclerosis is the most common cause of aortic valvular disease Syphilitic aortic disease has been discussed in Chapter 7 The diagnosis of rheumatic aortic insufficiency depends on a history of rheumatism and on associated mitral disease Arteriosclerotic aortic insufficiency is diagnosed by eliminating other possible causes of the lesion If there is associated aortic stenosis syphilis can be safely excluded Traumatic rupture of a semilunar cusp is a rare cause of aortic insufficiency and occurs only in a valve previously weakened by disease Aortic insufficiency is followed by marked enlargement of the left ventricle and eventually by left ventricular failure The rheumatic and syphilitic cases show the usual peripheral manifestations of

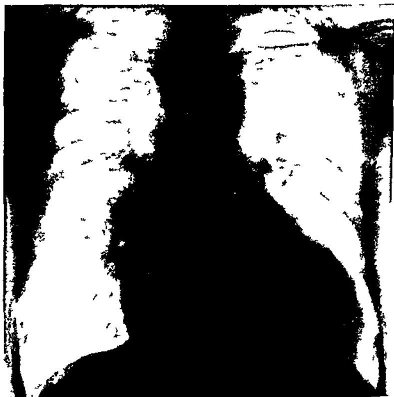


FIG 14—Chronic rheumatic valvular disease with aortic insufficiency Note great enlargement of the heart especially of the left ventricle

aortic insufficiency water hammer pulse high pulse pressure and so called capillary pulse Arteriosclerotic aortic insufficiency and functional aortic insufficiency are less apt to exhibit these changes in the peripheral circulation Aortic insufficiency due to atherosclerosis adds little to the gravity of the underlying disease and does not appreciably alter the clinical picture These patients are usually suffering from arterial hypertension or from atherosclerosis of the aorta and their future depends more on the progress of these conditions

Aortic Stenosis

Calcareous aortic stenosis may result from calcareous deposits in an old rheumatic valvular lesion or it may arise as a *primary arteriosclerotic process Rheumatic aortic stenosis is* usually associated with a mitral lesion there is often history of ancient rheumatic infection Arteriosclerotic aortic stenosis occurs in persons past 60 and chiefly in males it is a solitary valve lesion and there is no history of antecedent rheumatic infection Aortic stenosis does not result from syphilitic infection

The physical signs of rheumatic and arteriosclerotic aortic stenosis are identical A rough systolic murmur usually accompanied by a systolic thrill is heard and felt at the aortic area In the presence of heart failure the murmur may become soft and faint and the thrill may disappear Aortic stenosis presents symptoms different from those of other valvular lesions The syndrome of angina pectoris is common It is caused not by disease of the coronary arteries but by narrowing of the aortic valvular opening itself which impairs the blood supply to both coronary arteries simultaneously The presence of aortic stenosis should be suspected when a patient who for years has had a heart murmur or a valvular

lesion subsequently develops angina pectoris Sudden heart failure in these patients induces coronary insufficiency and is often followed by symptoms simulating coronary thrombosis Partial and complete heart block are also often associated with calcareous aortic stenosis These are caused by extension of the calcific process into the ventricular septum with involvement of the auriculoventricular bundle Sudden syncope is common in patients with aortic stenosis and death often comes instantaneously and unexpectedly The diagnosis of calcareous aortic stenosis can in a large number of instances be confirmed by visualizing the calcified aortic ring fluoroscopically when the observer's eyes have been fully accommodated

Treatment of patients with chronic valvular disease does not differ from that of other patients with heart disease The patient should keep his activities within the range set by his cardiac reserve and this is usually signalized by the appearance of dyspnea when he overtaxes himself Digitalis is given only when there is heart failure With the onset of heart failure the patient should be put to bed and treated by the usual measures Even in older persons with rheumatic valvular disease *heart failure may be induced by rheumatic carditis* accompanying a rheumatic reinfection Arthritis is rare and the temperature does not range high so the infection is difficult to recognize Its presence may be suspected when the patient does not respond to treatment

Cardiac Irregularities

Extrasystoles or premature beats are very common in older individuals they are usually ventricular in origin They may occur in hearts that are otherwise normal or may appear in hearts that are diseased As a rule they are of no clinical

significance They may result from tobacco coffee or digitalis intoxication

Their sudden appearance accompanying an acute infectious disease such as pneumonia or erysipelas gives evidence that the heart has been damaged by the toxins or virus of the disease Auricular extrasystoles in patients with great cardiac enlargement are usually forerunners of auricular fibrillation Numerous extrasystoles occurring in patients with arteriosclerosis of the coronary arteries particularly when associated with anginal attacks usually indicate a progressive vascular lesion Short runs of extrasystoles or multifocal extrasystoles in such patients at times may act as a trigger mechanism initiating ventricular fibrillation which is followed by sudden death

Extrasystoles as such require no treatment unless they disturb the patient or unless there is reason to fear the development of ventricular tachycardia or fibrillation It is the underlying heart condition that determines the treatment In the absence of demonstrable heart disease extrasystoles may be ignored If it is desirable to stop the irregularity this can usually be achieved by giving quinidine sulfate in doses of 3 gr three or four times a day At times digitalis 1½ gr twice a day may succeed when quinidine fails

Auricular fibrillation occurs in older patients as it does in the young in long standing heart disease with considerable cardiac enlargement particularly enlargement of the left auricle It is seen in patients with rheumatic hypertensive or arteriosclerotic heart disease Auricular fibrillation may appear suddenly as a complication of cardiac infarction In such cases there is often a spontaneous return to sinus rhythm As in younger patients auricular fibrillation occurs with hyperthyroidism and in elderly persons it may be the presenting sign of the thyroid disorder Finally there are cases in which

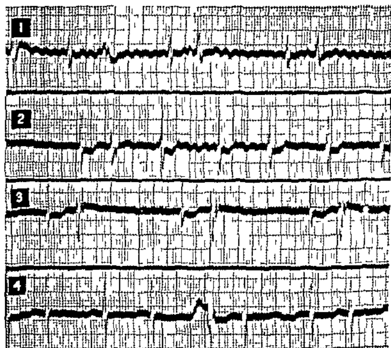


FIG 15 —Electrocardiogram Auricular fibrillation in a patient without demonstrable organic heart disease

auricular fibrillation is the sole evidence of cardiac abnormality It is not uncommon in older persons and has been called arteriosclerotic auricular fibrillation It is doubtful whether this designation is correct for there may be no gross evidence of arteriosclerosis and the condition is also encountered in younger individuals In the elderly auricular fibrillation without demonstrable associated heart disease causes little disturbance The ventricular rate is usually slow and there is little dyspnea or heart failure In itself it does not shorten life nor does it greatly impair the efficiency of the individual

The treatment of auricular fibrillation is the treatment of the underlying heart condition Digitalis should always be given in dosage sufficient to slow the ventricular rate to between 70 and 80 and to keep it at that level When the heart rate is rapid and there is much dyspnea and congestive failure large doses may be given at first 4 cat units twice a day for two days After this the dose should be adjusted to meet the needs of the patient Usually 1 or 2 cat units daily is the maintenance dose The medication must be continued indefinitely as long as the irregularity persists In elderly persons the heart rate can be controlled by small doses of the drug Often 1 cat unit every day or every other day is sufficient

Heart block complete or partial in elderly individuals is due almost invariably to myocardial fibrosis consequent to coronary artery disease Sudden development of heart block is often associated with infarction of the posterior wall of the left ventricle for with this lesion the blood supply to the auriculoventricular node may be affected Such heart block may be permanent or may recede in a few days Treatment is that of the underlying heart condition In the presence of partial heart block digitalis should be used with great caution or not at all It may convert partial into complete block In the presence of complete block digitalis may be used

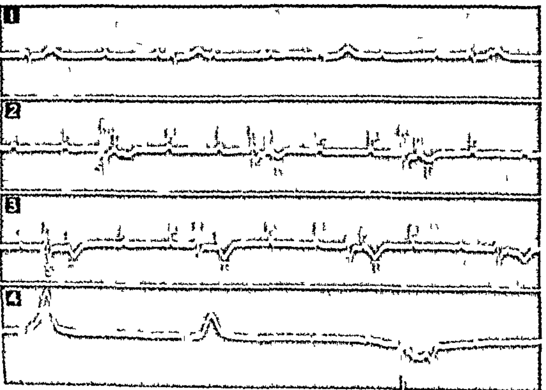


Fig. 10.—Electrocardiogram showing complete heart block



Fig 17 —Electrocardiogram Bundle branch block

freely to combat heart failure At times attacks of Stokes Adams syncope occur in these patients There is sudden cessation of the heart sounds the patient becomes unconscious and may have a convulsive seizure After periods of time varying from five to 60 seconds the heart resumes its beating and consciousness returns The Stokes Adams syndrome in some cases is due to ventricular standstill and in others to transient ventricular fibrillation It is important to try to differentiate between the two by taking an electrocardiogram during the attack If there is transient ventricular fibrillation the administration of quinidine sulfate, 3 to 5 gr every four hours, should stop the seizures In these cases adrenalin is dangerous for it may induce or favor ventricular fibrillation If the attack is due to ventricular standstill quinidine is useless Hypodermic injection of adrenalin 5 to 10 minims, usually arrests the attack The dosage should be continued at appropriate intervals depending on the frequency of the attacks Ephedrine hydrochloride ⅜ gr four times a day is often effective If these drugs fail, one may try barium chloride ½ gr three times a day With careful treatment the attacks of syncope can often be controlled Often the attacks are initiated by acute myocardial damage and if the patient can be tided over the acute period complete recovery may ensue

Bacterial Endocarditis

Bacterial endocarditis, both the acute and the subacute form is encountered with sufficient frequency among older persons to oblige the physician to suspect its presence in every case of obscure fever[1] Approximately 10 per cent of

[1] Zeman F D and Siegal S "Acute Bacterial Endocarditis in the Aged" Am Heart J 29 597 1945 Zeman F D "Subacute Bacterial Endocarditis in the Aged" ibid p 681 1945

all cases of subacute bacterial endocarditis occur in patients over age 50

Acute bacterial endocarditis is induced by one of the pyogenic bacteria that gains admission to the blood stream through some suppurative focus such as a pneumonia a breaking down carcinoma an infected kidney or mastoid or a carbuncle of the skin The presence of diabetes often accelerates such infection and the existence of a heart valve damaged by an ancient rheumatic infection favors the lodgment of bacteria Vegetations may develop on healthy valves The pneumococcus is one of the organisms most frequently encountered in acute bacterial endocarditis in older persons As a rule the primary infection in the lungs kidneys or elsewhere dominates the clinical picture and the diagnosis is overlooked Examination of the heart may reveal only a systolic murmur the significance of which is difficult to evaluate in older persons Petechiae or other emboli or an enlarged spleen may suggest the presence of endocarditis The diagnosis will be made only if blood cultures are made in the presence of sepsis particularly when associated with chills Positive results of a blood culture usually indicate bacterial endocarditis

Intensive administration of penicillin as outlined in the following section on subacute bacterial endocarditis offers some hope of cure At the same time attempts should be made to drain or eliminate the primary focus of infection

Subacute bacterial endocarditis is caused by infection with Streptococcus viridans enterococcus or Hemophilus influenzae With rare exceptions these organisms induce inflammatory vegetations only on valves damaged by previous disease Even in elderly persons the most common antecedent lesion is rheumatic valvular disease although infection may occur on syphilitic or arteriosclerotic valves and in rare cases on a

congenital anomaly with which the patient has survived to an advanced age The clinical picture commonly resembles that seen in younger persons A patient with a valvular defect has fever possibly chills embolic phenomena such as petechiae red blood cells in the urine infarcts of the spleen kidney or brain enlargement of the spleen clubbing of the fingers Blood culture reveals the infecting organism In such typical cases the diagnosis *is simple if the clinician will recall* that the disease occurs in older persons The clinical picture may be more obscure Low grade fever may be the only presenting sign Murmurs in old people are always difficult of interpretation and are too apt to be dismissed as being *due to arteriosclerosis of the valves Heart failure may over* shadow the other symptomatology Only a positive blood culture makes the diagnosis definitive If the blood culture at first is negative it should be repeated several times for often the organism grows with difficulty on artificial mediums

Healed subacute bacterial endocarditis a condition in which there have been spontaneous healing and sterilization of the valvular vegetations presents a different clinical picture The patient has a darkly pigmented skin there may or may not be fever with occasional emboli There are *spleno*megaly renal insufficiency with azotemia and progressive anemia Blood cultures remain negative

Treatment With penicillin some 75 per cent of patients with subacute bacterial endocarditis can be cured of their *infection Some die of embolism or heart failure* Dosage of the drug should be carefully planned for insufficient initial dosage may make the infecting organism resistant to penicillin and so prevent a cure inadequate total dosage temporarily arrests the infection *but* permits a recurrence when *treatment is stopped* The first step is to determine the degree of resistance to penicillin of the infecting organism The dos

age is adjusted to the coefficient of resistance as set forth in Table 5

TABLE 5 —DOSE OF PENICILLIN FOR ORGANISMS WITH VARYING COEFFICIENTS OF RESISTANCE*

COEFFICIENT OF RESISTANCE OF ORGANISM	DOSE BY INTRAMUSCULAR INJECTION EVERY 3 HOURS	PEAK BLOOD CONCENTRATION TO BE ACHIEVED IN UNITS PER CC BLOOD SERUM
1	15 000	0 5
2–3	25 000	1 0
4–5	50 000	2 0
5–10	100 000	6 0
10–20	200 000	11 0
20–30	300 000	16 0

* From G[illegible] be I E [illegible] P[illegible] tr t on of Pen ill n nt F [illegible] f Inf ct J A M A 130 761 1946

It is well to give additional doses of from 50 000 to 100 000 units twice a day The whole purpose is to maintain blood levels of penicillin that will destroy the infecting organism Such large doses bring about peaks of high penicillin blood levels Intramuscular administration is more effective than intravenous injection Treatment should be continued for at least four weeks Usually the fever and the active symptoms are controlled within a few days but prolonged treatment is essential to make certain a permanent cure

Organisms that are more than 30 times as resistant as the standard strain of staphylococcus rarely can be eliminated by treatment with penicillin In such cases streptomycin may be successful I have seen several patients with highly resistant enterococcus infection cured with streptomycin

Chapter Nine

DISEASES OF THE CARDIOVASCULAR SYSTEM—GENERAL MANAGEMENT

THE TREATMENT of the patient with a diseased heart is not a simple matter It involves more than knowing when and how to administer digitalis It demands first of all an accurate and complete etiological physiological and anatomical diagnosis It calls for understanding and patience to grasp the patient s many problems and to help him readjust his whole life to the functional capacity of his damaged heart It predicates a comprehension of the unique relationship between heart and psyche through the intermediation of the vegetative nervous system Finally it demands an unwavering faith in the efficacy of treatment and in the astounding recuperative power of the heart So often by calling on its last ounce of reserve does the failing heart re establish the circulation and give the patient a fresh hold on life that there is hardly ever justification for the verdict "This case is hopeless The admission of defeat encourages defeat

We shall first discuss the management of patients with arrested or slowly progressing heart lesions that do not limit physical activity or at most give rise to slight symptoms on greater activity

The patient should be told that he has a cardiac abnor

mality but he must be made to understand that the lesion does not endanger life that it merely calls for reasonable caution The heart is quite able to meet the demands made by the ordinary exigencies of life but has not the reserve power to withstand greater and extraordinary drains upon its strength In perfect health the heart can take care of all the needs of the body In the presence of a damaged heart body activity should be adapted to the cardiac capacity in deed should be kept at a level a bit below that capacity The measure of the strength of the heart is its response to effort Heart strain is signalized by the subjective symptoms of dyspnea palpitation and precordial pain The amount of effort required to provoke these symptoms is a gage of cardiac reserve power

But dyspnea palpitation and precordial pain may occur also with functional neurogenic disturbances of the circulation obesity or severe anemia To be indicative of early heart failure these symptoms must be associated with a cardiac lesion capable of provoking them or with physiological disturbances of the heart such as alterations in rate or rhythm When a neurogenic cardiovascular disturbance is superimposed upon an organic lesion the interpretation of the symptoms may be difficult Women with hypertension often complain of hot flushes vertigo rapid palpitation dyspnea and sticking precordial pain determined by a neurogenic disorder

In such patients the symptoms are out of all proportion in their *intensity to the anatomical changes in the heart* Were they determined by heart failure one would find a large dilated heart distended neck veins cyanosis and congestion of the lungs or liver Instead the heart is small and there is no venous congestion The symptoms must always be correlated with the heart lesion In patients with psychoneurotic disturbances manifesting themselves in a cardio

vascular symptomatology, the erroneous diagnosis of heart failure and the restrictions and treatment consequent thereon may do incalculable harm

Thus the first task of the physician is to enlist the patient's aid in working out his exercise tolerance This is best achieved *by studying his response to his regular daily mode of life* If the patient can carry on without any symptoms, his cardiac reserve is excellent and his activities need not be curtailed If certain efforts, such as climbing stairs carrying heavy parcels or sweeping give rise to discomfort or induce undue fatigue or if the patient is exhausted in the evening after his round of duties he is overstraining himself and his heart In many instances merely slowing the tempo of activity enables the individual to carry on without distress The patient must learn to regulate the amount and vigor of his movements to a point below that which will give rise to symptoms Thus if climbing two flights of stairs brings on shortness of breath he should if he must ascend two stories rest after the first flight so that the second one may be negotiated without discomfort

Climate and Altitude

Climate —This has little direct influence on the progress of heart disease and there are no general rules applicable to all patients Insofar as climate contributes to respiratory infections it is of great importance for rheumatic recrudescences are often initiated by such infections and in all forms of heart disease the load placed on the circulation by an attack of bronchitis or bronchopneumonia may precipitate heart failure This last complication is to be feared particularly in patients with advanced pulmonary emphysema The winters in the Middle Atlantic states and in New England, with their great variations in temperature and moisture are a real

hardship to individuals with damaged hearts A warm equable climate such as is found in the South is to be preferred indeed it is almost mandatory for those with more advanced lesions who are particularly susceptible to colds and respiratory infections If there has been no heart failure the necessity for a change of climate is not so exigent It is usually preferable to permit the patient to continue the normal routine of his life rather than subject it to such violent dislocation as is usually entailed by a winter move to the South If in addition to the cardiac affection there is a chronic sinus infection the moist climate of the southern seaboard may be unfavorable In such cases the dry warmth of Arizona or New Mexico may be more beneficial Patients with angina pectoris always have greater difficulty in cold windy weather Many feel quite well during the summer but when winter comes find their activities greatly restricted because of the frequent occurrence of anginal attacks in cold blustery weather For them a warm climate is very helpful and comforting

There are some who do not tolerate heat particularly women with hypertension They experience flushes headaches palpitation and increased weakness at higher temperatures Florida climate does not agree with them

Altitude —The rarefied atmosphere at high altitudes causes anoxemia which may be of sufficient degree to burden the heart The chief evidence of such heart strain is an increased pulse rate markedly exaggerated by slight exertion Cardiac dilatation may ensue Such effects are produced at altitudes of 14 000 ft or more rarely at lower levels

Patients with heart disease have a fear of altitude and their physicians often counsel them against spending a summer in the mountains Altitudes up to 6 000 or 7 000 ft have no effect upon the heart Indeed some claim that such heights benefit certain forms of heart disease Sojourns in mountain

ous country rarely injure subjects of heart disease because of the altitude as such but rather because the nature of the terrain may compel them to do too much climbing

The patient with organic heart disease need not avoid moderate heights such as are found in the Adirondacks the Catskills or the Appalachians but he should avoid undue climbing which even at lower levels may strain his heart The choice of a summer resort or of a permanent home need not be dictated by the condition of the heart

Airplane flights not exceeding 10 000 ft in height are not injurious to the heart by reason of the high altitude The psychic influence of the excitement of taking off or the effects of air sickness may far outbalance any possible effect induced by the rarefied atmosphere Whether a patient with heart disease may undertake an airplane flight depends chiefly on his psychic make up The stratosphere flights of the future will probably be taboo

Anesthesia and Operation

Contemplation of operative intervention in a patient whose heart is diseased calls for an evaluation of the added risks that the cardiac condition introduces into the surgical procedure Misjudgment results when heart disease is regarded as a unitary disorder A variety of diseases affect the heart and their effects on cardiac function differ at different periods of their evolution Clarity of appraisal is reached with the recognition that there is no one form of heart disease but that there are heart diseases as well as hearts with different degrees of functional capacity

The cardiac disease hardly increases the operative mortality in patients who have no history or evidence of heart failure but have chronic rheumatic valvular disease uncom

plicated essential hypertension or heart disease due to hyper thyroidism or congenital defects For this group of patients the criteria for anesthesia and operation are practically the same as for normal individuals The operative mortality hardly exceeds that of normal individuals They may be sub jected to emergency operation without fear Operations of choice such as herniotomies and cholecystectomies may be carried out There is much to be said for operating early while the heart is still well compensated Delaying until the condition has become advanced may necessitate operation at a time when the heart has begun to fail In these patients there is no need for the pre or postoperative administration of digitalis Fluids may be given freely both by mouth and intravenously

Patients with coronary artery sclerosis and with syphilis of the aorta and aortic valves are less favorable subjects for sur gery A recent study revealed an unexpected operative mor tality of 8 per cent All but urgent operations should be avoided The expectancy of life of these patients is short and the need for operation should be balanced against the prog nosis for the heart condition If operation becomes necessary a short anesthesia speedy operation and minimal trauma and bleeding must be assured In these patients an unfore seen coronary thrombosis may develop at any time even as late as several weeks after the operation The frequency of this association is such as to render a causal connection prob able Patients with these forms of heart disease are subject to sudden death due presumably to ventricular fibrillation This seems to occur more frequently when there is a pre existing extrasystolic irregularity To such patients it may be wise to give 3 gr of quinidine sulfate three or four times a day for several weeks

For patients with congestive heart failure operation is

hazardous and should be resorted to only as a life saving measure These patients show an unexpected mortality of 17 per cent Here is need for a surgeon of real virtuosity There is little time for preoperative preparation of the patient The most important measure is the speedy administration of full doses of digitalis If the patient has had no previous medication with digitalis he may be given 1 2 mg of digitoxin (Digitaline Nativelle or Purodigin) by mouth This is the full digitalizing dose The maintenance dose is 0 2 mg a day Or else 20 gr or 15 cat units of digitalis leaf may be given in divided doses in 24 hours The maintenance dose is from 1 to 2 cat units a day If there is much venous congestion a phlebotomy of 300 to 500 cc may be helpful In these patients the administration of fluids intravenously may place too great a strain on the heart and may even precipitate an attack of pulmonary edema This happens more often with the transfusion of blood than with the infusion of saline When it becomes necessary to administer fluids intravenously or to give a transfusion, the injection should be given slowly by the drip method and the patient should be kept under constant observation Of the supplementary cardiac stimulants caffeine sodium benzoate 7½ gr given every three to four hours is best Restlessness should be combated with morphine and appropriate sedatives In the presence of much dyspnea and cyanosis oxygen quiets the patient and eases the work of the heart

The presence of auricular fibrillation as such does not materially add to the operative risk provided the heart rate is kept under control Enough digitalis should be given to maintain the ventricular rate as counted with the aid of a stethoscope—between 70 and 80 beats a minute Measurement of the pulse rate at the wrist is inaccurate because of the common presence of a pulse deficit Auricular fibrillation as a

rule develops in the late stages of heart disease so that it occurs in the more badly damaged hearts except in patients with hyperthyroidism

When circulatory embarrassment is induced or exaggerated by a condition amenable to surgical treatment operation is imperative It offers the only chance of relieving the heart of its extra burden and of restoring compensation The commonest condition of this type is hyperthyroidism which has either directly led to the heart disease or has aggravated some form of preexisting heart disease Congestive heart failure is seen only in cases that persist over many years It is rather uncommon and occurs almost exclusively in patients who have coexistent organic heart disease

At times a damaged heart is further weakened by the presence of severe secondary anemia occasioned by bleeding fibroids hemorrhoids or some analogous condition In these cases the anemia as such contributes to the heart failure so that there is definite indication for operation to arrest bleeding Preoperative treatment with bed rest digitalis diuretics and particularly transfusion to restore the normal oxygen carrying capacity of the blood will bring about sufficient improvement to make operation possible Transfusions of citrated blood may be given—very slowly by the drip method—even in the presence of heart failure It is wiser to give small quantities 250 cc daily rather than to attempt to administer 500 cc at a time

In all operations on patients with heart disease pre and postoperative care must be meticulous particular attention should be given to the prevention of preoperative anxiety and to cardiac strain incident to the excitement stage of anesthesia A highly skilled anesthetist is always required In selected cases local anesthesia may be best in many avertin (tribromethanol) is most satisfactory as a basal anesthetic

Chloroform which is little used in this country is best avoided because of its known tendency to induce ventricular fibrillation Spinal anesthesia as a rule is not adapted to cardiac patients because of the drop in blood pressure that so often ensues This is particularly marked in individuals with arterial hypertension and in them spinal anesthesia should be avoided Most patients with cardiac disease tolerate ether well and in most instances it is the best anesthetic In the presence of emphysema and bronchitis ethylene or cyclopropane is better borne than ether

Often the nervous tension incident to anticipation of the operation quickens the heart rate to a level higher than that provoked by the operation itself This occurs particularly when the patient is brought into the operating room fully conscious and the anesthesia is started with the patient on the operating table Again the excitement stage of the anesthesia whether it be nitrous oxide ether or ethylene is always accompanied by a great rise in heart rate which usually exceeds the maximum rate during operation as well as that induced by preoperative excitement Fluctuations in rate are closely linked to the depth of anesthesia when the anesthesia becomes light the heart rate quickens In a placid individual local anesthesia is often associated with a remarkable stability of heart rate In avertin anesthesia the excitement stage with rapid pulse is usually avoided During the operation itself the heart rate is usually remarkably constant and is little influenced by manipulations of tissues or viscera unless great hemorrhage or shock sets in Anesthesia may cause abnormalities of cardiac mechanism such as extrasystoles or paroxysmal auricular tachycardia These are of little clinical significance for they almost invariably subside spontaneously

Heart Failure

The treatment of heart failure is the same no matter what the age of the patient Symptoms of heart failure whether they be dyspnea cough edema or chest pain are evidence that the heart is overtaxed The first principle is to relieve the heart of all unnecessary strain To rest the heart one must rest the body so the first indication is to put the patient to bed *Bed rest should be continued until the evidences of* heart failure have subsided Digestion just like bodily activity increases the work of the heart so the diet should be kept light and scanty

In chronic heart disease with recurring heart failure the patient s appetite is poor and he is apt to suffer from chronic undernutrition His protein intake has usually been low for weeks or months often to such an extent that the level of blood proteins is reduced In the absence of complicating renal disease very low figures are not reached but levels of 5 5 to 6 Gm per 100 cc of blood are common This lowered blood protein level favors the development of edema particularly with the rise in venous pressure that accompanies heart failure It is well therefore to prescribe a diet high in protein Often the administration of thiamine hydrochloride 3 mg twice a day and nicotinic acid 50 mg three times a day seems to be helpful

In all cases of heart failure efforts should be made to control abdominal distention which by pushing up the diaphragm may embarrass the heart With the onset of heart failure urinary excretion diminishes and there is retention of fluid in the body which may eventually cause an increase in blood volume and thus increase the work of the heart Control of the fluid exchange of the body is fundamental to the treatment of heart failure

The fluid intake should be restricted to 1 000 cc in 24 hours The fluid intake and the urinary output should be recorded daily to enable the physician to follow the course of the fluid balance of the body *Often* with rest and fluid restriction alone heart failure subsides and compensation is restored This can be hastened by the administration of digitalis In mild cases 1 cat unit of digitalis or 0 2 mg of digitoxin twice a day is sufficient If heart failure is severe and if the patient has had no digitalis medication he may be digitalized rapidly The average full digitalizing dose is 20 cat units of the leaf or 1 2 mg of digitoxin This is only a rough guide for there is great individual variation among patients in the doses of digitalis that they need and that they will tolerate For rapid digitalization it is best to give 1 2 mg of digitoxin in one dose Digitalis leaf should be given in divided doses to avoid nausea induced by direct irritation of the stomach The maintenance dose too varies with the individual When given over long periods of time 0 2 mg of digitoxin or 1 cat unit daily is often sufficient In the presence of auricular fibrillation the dosage is easily regulated The ventricular rate is used as a guide and enough drug is given to maintain the ventricular rate between 70 and 80 a minute When the rhythm is regular the heart rate is no guide to dosage Old people as a rule respond to smaller dosages of digitalis than do the young and are more apt to develop toxic poisoning The appearance of extrasystoles particularly of coupled beats is definite evidence of digitalis intoxication With the first appearance of such signs the drug should be discontinued until they have subsided With proper control vomiting should rarely appear

When bed rest limitation of fluids and digitalis do not bring rapid relief recourse should be had to diuretics Caffeine and theobromine have a rather feeble diuretic action

and are rarely used Aminophylline is more powerful and may be given in doses of 1½ to 3 gr three times a day for a few days When its use is continued too long it loses its effect *Better than aminophylline is ammonium chloride given in* the form of the 7½ gr enteric coated tablet Three to four such tablets should be given three times a day If a still more powerful diuretic is needed 1 or 2 cc of one of the mercurial diuretics may be given intravenously or intramuscularly If kidney function is good the dose may be repeated every three to five days depending on the degree of water retention The administration of ammonium chloride for 24 hours preceding the injection enhances the action of the mercurial diuretic

Paracentesis of the chest or abdomen is rarely indicated since mercurial diuretics have come into use However when the aforementioned measures do not relieve pleural effusion or ascites the fluid should be withdrawn particularly when it is causing distress by its mechanical presence

After recovery from gross heart failure the patient should be allowed to resume his activities very slowly and guardedly Incautious haste may result in recurrence of heart failure After a major episode of heart failure a four week rest in bed should be prescribed even when the symptoms subside promptly Return to full activity should be guided by the patient s reaction to physical exertion

Cardiac Psychoses

Serious psychoses occurring as complications of heart disease are not common It is assumed that they are caused by inadequate nutrition of the brain resulting from the disordered circulation They appear particularly in older persons with latent or frank cerebral arteriosclerosis In such persons heart failure may upset the balance of the cerebral circulation

to such an extent that serious cerebral anoxemia follows Many patients with chronic cardiac disease eat so poorly for long stretches of time that actual dietary deficiencies may occur In such patients pellagrous mental changes may develop Rarely digitalis may induce a psychosis

The psychic disturbance may manifest itself in several ways and during various stages of the cardiac disorder Most commonly it appears a few days prior to death but it may occur many weeks before It is usually a sign of grave prognostic import, although certain patients recover The usual picture is that of a grave depressive psychosis Commonly, the patient is convinced that the doctors and nurses wish to do him harm, often he fears poisoning and refuses all food and medication As a result of his delusion he may become greatly excited in an endeavor to escape from his persecutors or he may attempt suicide Accompanying the delusions there may be visual and auditory hallucinations The motor excitement and restlessness often place a great and deleterious strain on the damaged heart

Usually the psychic disorder develops during grave myocardial insufficiency and persists with occasional lucid intervals until death In some instances however with the recovery of cardiac function the psychosis disappears It may develop during convalescence from an attack of heart failure and under such circumstances has been attributed by some authors to the resorption of the edema fluid

In a masterly manner Head[1] has described the lesser mental changes that often accompany disease of the lungs or heart Loss of memory and attention is common Characteristic are hallucinations of vision which usually take the shape of an indistinct draped human form at the foot of the bed

1 Head H "Certain Mental Changes That Accompany Visceral Disease" Brain 24 345 1901

and are white black or gray never in color This distinguishes them from hallucinations of the insane which are usually colored Hallucinations of hearing never include articulate voices but assume the form of tapping knocking or of bells Hallucinations of smell are usually accompanied by nausea In addition patients may experience paroxysms of depression which come on inexplicably Many are haunted by a vague fear of impending misfortune In time this mood is followed by a feeling of suspicion that they are being neglected or harmed by their attendants and former friends Head found that in every case the only constant factor that accompanied these mental disturbances was referred visceral pain Other factors too play a role for women are affected three times as frequently as men The explanation of these phenomena can be given best in Head s own words

> Under normal circumstances visceral life takes place outside consciousness Reflected pain of visceral origin brings in its train all those images and dispositions which exist normally at the fringe of or entirely outside the field of consciousness All those sensations that are associated with visceral activity which do not exist in consciousness under normal conditions come to the surface The patient s character appears to be altered for the content of his consciousness is changed He will become moody at one time unduly exalted at another depressed without cause Reason is displaced and he is the victim of each passing wave of feeling tone and he will have lost control over the expression of his emotions and of his temper
>
> That barrier which the normal mind sets between conscious life and that of the viscera the integrity of which depends on a high potential of vitality in the nervous system has been broken down

The treatment of cardiac psychoses is primarily treatment of the accompanying heart failure Oxygen should always be given to lessen cerebral anoxemia When there is reason to suspect dietary insufficiencies nicotinic acid should be given

by mouth or intravenously 300 to 500 mg a day If there is no improvement within two or three days the drug should be discontinued With improvement the medication should be continued, but after the first week 50 mg three times a day is sufficient

Thrombophlebitis of the Leg Veins and Pulmonary Embolism

Pulmonary embolism arising from a thrombus in the veins of the legs is a common and hazardous complication in bed ridden patients who are over the age of 50 It occurs not only after operations but in all kinds of illnesses, particularly in the obese and in patients with heart failure Thrombophlebitis of the veins of the lower extremities and of the pelvis becomes increasingly common with advancing years Barnes[2] reported that at the Mayo Clinic 70 per cent of patients who died of postoperative pulmonary embolism were over 50 years of age and that only one was less than 30 Hunter[3] found thromboses of the calf veins in 53 per cent of 351 cases seen at autopsy The average age of the persons with venous thrombosis was 65 In over one half of the cases the veins of both legs were involved Of the cases with venous thromboses 5 per cent had fatal and 20 per cent nonfatal pulmonary emboli Somewhat over 2 per cent of all deaths of patients in hospitals are due to pulmonary embolism

The chief factor responsible for peripheral venous thrombosis and subsequent pulmonary embolism is bed rest The more immobile the patient, the more readily does thrombosis

[2] Barnes A R "Pulmonary Embolism" J A M A 109 1347 Oct 23 1937

[3] Hunter W C *et al* "Thromboses of the Deep Veins of the Leg" Arch Int Med 68 1 July 1941

occur Thrombi may form after a few days of confinement In England not a few cases were encountered in elderly people who were compelled to sleep in cramped positions in air raid shelters Operation and traumatic injuries are common antecedents of thrombosis and embolism It is not generally recognized that heart failure is one of the chief causes predisposing to thrombophlebitis and pulmonary embolism Venous thrombosis and embolism are so common in bed ridden cardiac patients that they should always be watched for Thrombophlebitis is more frequent in the winter and in cold climates

Immobility as well as heart failure lead to slowing of the blood stream in the peripheral veins The venous blood stream is maintained by the arterial head of pressure by the contractions of the muscles by free respiration which creates a negative pressure in the thorax and by the descent of the diaphragm which milks blood out of the abdominal structures All of these factors are reduced by immobility in bed and the flow of blood is further retarded by shock or by cardiac insufficiency

Fully 95 per cent of venous thromboses occur in the deep veins of the calf From here the thrombus extends up to the femoral and external iliac veins More rarely the pelvic veins or the prostatic venous plexus is involved When one of the larger more superficial veins is thrombosed the diagnosis is easy There are pain swelling and tenderness along the affected vein the leg becomes swollen and the overlying skin may be reddened The patient develops fever More often than not these gross evidences of venous thrombosis are lacking the patient may complain of a little pain in the calf of the leg and a pulmonary embolus first calls attention to the peripheral venous thrombosis Only by careful daily observation can an early diagnosis be made Many cases run

their course with minimal or no pain and no local swelling. The calf or thigh muscles may be tender to pressure measurement of the circumference of the legs may reveal slight enlargement of one extremity there may be slight fever and leukocytosis The sedimentation of the red blood cells is usually accelerated Roentgen visualization of the veins after injecting a radiopaque substance into the vein at the ankle has not lived up to its early promise as a diagnostic procedure The films are difficult to interpret and often lead to erroneous conclusions

Often a pulmonary embolus gives the first warning of the presence of thrombophlebitis The occurrence of a pulmonary embolus is presumptive evidence of thrombophlebitis of the veins of the legs and calls for careful examination of the legs Even in the absence of physical signs the presence of thrombophlebitis in the legs should be assumed unless there is another patent source of the embolus

The symptoms of pulmonary embolism are rarely the classic ones of hemoptysis and pleural friction rub followed by consolidation of the lungs Even dyspnea is not a constant sign The chief evidences are sudden shock faintness sweating and a rapid pulse Often weakness and anxiety are the sole symptoms There may be chest pain, usually in the axilla Hemoptysis is relatively infrequent and lung signs may or may not develop Roentgenography of the chest should be freely used as an aid in diagnosis A rise in temperature is the rule The first embolus is usually a small one One or more of such nonfatal embolic episodes usually precede a lethal attack Pulmonary embolism occurs in about one of three patients with thrombophlebitis and in one of 25 cases the attack is fatal

In certain cases the textbook signs of dyspnea pulmonary consolidation and hemoptysis develop Bronchopneumonia

is often erroneously diagnosed A massive embolus may cause instantaneous death A large nonfatal embolus gives rise to the signs and symptoms of acute cor pulmonale characterized by acute dilatation and strain of the right ventricle In such cases there is marked dyspnea often with cyanosis Increased cardiac pulsation may be visible in the second and third interspaces to the left of the sternum in the region of the conus of the right ventricle A systolic murmur is audible in this area and the pulmonic second sound becomes accentuated The electrocardiogram may show a characteristic pattern with an S wave in lead 1, the ST segment depressed the T wave diphasic in lead 2 and the RT segment elevated and the T wave negative in lead 3 There is usually a Q wave in lead 3 The electrocardiogram may be confused with that of an infarct of the posterior wall of the left ventricle If the patient recovers the electrocardiogram returns to its original pattern

Treatment —Prevention of thrombophlebitis of the veins of the legs is possible in a large proportion of cases Measures should be directed to preventing slowing of the venous return flow from the legs Elderly persons should not be confined to bed more than is absolutely necessary when in bed they should be encouraged to move about freely and if they are disabled their position should be changed frequently They should be compelled to flex and extend their feet legs and thighs several times a day and if this is impossible they should be given centripetal massage of the legs twice daily Frequent deep breathing exercises should be encouraged Heart failure should be actively combated

Thrombophlebitis is so common in older debilitated patients that some experienced surgeons recommend prophylactic bilateral femoral ligation before operation for all patients over 65 There is much to be said for this procedure

If thrombophlebitis of the leg veins develops despite prophylactic treatment and more particularly if a pulmonary embolus occurs even in the absence of physical signs of thrombophlebitis immediate active intervention is indicated.[4] If the site of the thrombosis is known the superficial femoral vein of the corresponding leg should be exposed and opened the thrombus removed by suction and the vein divided between ligatures. Often it is necessary to do a bilateral femoral vein ligation because it is impossible to determine which veins are involved. Indeed this is probably the wisest routine procedure in all cases for the thrombosis is so commonly bilateral.

If the site of the thrombosis cannot be determined or if for some other reason operation is not feasible consideration should be given to the use of anticoagulants to arrest upward extension of the thrombus. The best preparation is heparin. It has the disadvantages that it is very expensive must be given intravenously and requires constant check on the coagulation time of the blood. It may be given in intermittent doses of 100 mg three times a day, or approximately the same quantity may be given by intravenous drip throughout the 24 hours. The dosage should be adjusted to maintain the clotting time of the blood between 30 and 45 minutes. Heparin prevents extension of the thrombus but it is difficult to know how long to continue treatment. A week is probably the minimum time. In several of my cases there was renewed extension of the phlebitis after the administration of heparin had been stopped. Again resumption of treatment promptly arrested the venous thrombosis. Dicoumarin an anticoagulant that can be given by mouth and is inexpensive is still in the experimental stage. Its administration must be carefully

[4] Allen, A. W., *et al.* Venous Thrombosis and Pulmonary Embolism, J. A. M. A. 128:397, June 9, 1945.

controlled by determinations of the prothrombin in the blood.

When there is massive pulmonary embolism [illegible] gr of papaverine hydrochloride should be given intravenously at once and repeated if necessary. This helps release secondary spasm in the pulmonary artery. Morphine should be administered to allay pain and oxygen to ease the respiration and relieve anoxemia. Subsequently full doses of digitalis should be given to combat heart failure. In all cases of pulmonary embolism sulfadiazine or penicillin should be given at once because bronchopneumonia is an inevitable complication.

Chapter Ten

DISEASES OF THE LUNGS

PULMONARY EMPHYSEMA

TWO TYPES of pulmonary emphysema are distinguished senile or nonobstructive emphysema and essential or large lunged emphysema

Senile emphysema is encountered in older individuals and has been interpreted as reflecting a degenerative process of the lungs When the thorax is opened at autopsy the lungs collapse They are small friable and anthracotic Microscopic examination reveals broken down and enlarged pulmonary alveoli with atrophy of the septa and no increase in the elastic tissue of the lung The chest is not large not barrel shaped The spine is straight and there is a degenerative change in the intervertebral disks This elevates the ribs and increases the size of the thoracic cage and alters the position of the lungs Kountz and Alexander[1] believe that the skeletal change is the primary one Calcification and ossification of the costal cartilages and ankylosis of the costovertebral joints are often marked The diaphragm is not depressed and the diaphragmatic excursions may be extensive Indeed in senile emphysema in contrast to the essential form the pa

[1] Kountz W B and Alexander H I "Nonobstructive Emphysema" J A M A 100 551 Feb 25 1933

tient s breathing is largely abdominal effected by the action of the diaphragm rather than by the intercostal muscles Interference with respiratory function is less than in essential emphysema There is no past history of lesions inducing bronchial obstruction However the several processes lead to the same physiological end result as that which takes place in essential emphysema a progressive impairment of the respiratory function and the vital capacity

Essential emphysema commonly first manifests itself in younger persons often at the age of 40 The lungs are large and voluminous pushing the diaphragm down elevating the ribs and covering the anterior aspect of the heart Large bul lae representing huge air sacs are often seen particularly along the anterior lung margins Microscopic examination re veals broken down and enlarged alveoli with much secondary increase of elastic tissue fibers The bronchi are usually in flamed and injected and may be dilated The chest is deep and *wide and the spine is curved into a kyphosis so that the* chest assumes the classic barrel shape The neck is short the scapulae ride high Calcification of the costal cartilages progresses with the years Because of the large volume of the lungs displacing the diaphragm downward the diaphragm moves very little with respiration Respiration is effected largely through contraction of the intercostal muscles and the accessory muscles of respiration and the costal margins move inward with each breath Because of the structural altera tions of the lung tissue which make it less efficient as a me dium for the exchange of gases between the alveoli and the blood and because of the loss of elasticity of the lungs and the impaired mechanism of the respiratory musculature there results marked impairment of respiratory function The two chief manifestations of this are dyspnea and cyanosis The chronic anoxemia resulting from the impaired respiratory

function leads to secondary polycythemia The blood volume is not increased and the hemoglobin and red cell contents do not reach the levels encountered in primary polycythemia The hemoglobin content rarely rises above 110 per cent and the red cells do not exceed 6 500 000 per cu mm The obliteration of much of the capillary bed in the lungs due to atrophy and destruction of the alveolar septa increases the peripheral resistance in the pulmonary blood circuit and increases the blood pressure in the pulmonary arterial tree This leads to atherosclerosis in the pulmonary arteries in both the large and the small vessels The work of the right ventricle is augmented so that in the course of time hypertrophy and dilatation of this chamber of the heart occur Eventually right heart failure with tricuspid insufficiency and dilatation of the right auricle may ensue

In both senile and essential emphysema hereditary factors are very evident so that one encounters multiple cases in families The development of essential emphysema is favored by the occurrence of pulmonary infections and by lesions which cause partial obstruction of smaller bronchi Thus emphysema is an invariable sequel of persistent bronchial asthma and commonly follows recurrent attacks of bronchitis

The symptoms of senile and essential emphysema are identical varying only in degree so they will be discussed together Senile emphysema is much slower in its evolution and for years leads to little impairment of respiratory function

The appearance of the patient with fully developed emphysema is so typical that it makes the diagnosis self evident One sees a middle aged man with high color often cyanotic puffing on slight exertion and subject to frequent cough The chest is deep and broad the neck short the back curved and the shoulders stooped forward The neck veins are full The finger nails show increased incurvation and often there is

true clubbing of the fingers There is little or no abdominal component of the respiratory movement the epigastrium does not move out with each inspiration The chest moves up and down as though in one piece

Percussion yields a hyperresonant tympanitic note all over the lung fields The areas of cardiac flatness and dullness are obliterated by the interposition of the voluminous lung between the heart and the anterior chest wall The diaphragm is pushed down so that pulmonary resonance extends below the tenth rib posteriorly The general hyperresonance obscures lesions that in a normal chest would give rise to dullness or flatness Thus infiltration or fibrosis of the lung or even a pleural effusion of moderate size is easily missed in a markedly emphysematous chest

Auscultation yields the characteristic sign of pulmonary emphysema namely prolonged expiration By watching the patient one sees that inspiration is quick and short expiration lengthy The respiratory note is low pitched and soft and in advanced cases may be almost inaudible Commonly wheezing and sibilant rales are scattered throughout the chest and at the bases posteriorly sticky moist rales are often heard Complicating bronchitis the condition that so often sends the patient to the doctor accentuates all of these signs Expiration becomes still more prolonged the breath sounds are fainter and rales of all sorts are found widespread in both lungs from apex to base At times they may be restricted to one lower lobe

The roentgen picture too is typical The lung fields are clear and brightly illuminated they do not become darker on expiration and the shadow of the heart and great vessels stands out clearly in contrast The clavicles are high and intercostal spaces wide and horizontal The dome of the diaphragm is flattened and its excursions greatly diminished

Physical signs referable to the heart are difficult to elicit The size of the heart cannot be mapped out because of the general hyperresonance the heart sounds are dulled and distant because of the cushion of lung interposed between it and the chest wall In normal chests that are not too thick walled the quality of the heart sounds gives a significant indication as to the state of the heart muscle This is not so in the presence of emphysema In such patients an accurate cardiac diagnosis cannot be made without use of the fluoroscope and the electrocardiograph Such examinations are all the more important because of the frequent association of arteriosclerotic heart disease and pulmonary emphysema.

The chief symptoms are dyspnea and cough At first the cough is noted chiefly in the morning on arising and is relieved when the accumulated nocturnal secretions have been expelled Gradually through the years the cough becomes more persistent and continuous and the dyspnea more disabling In advanced cases it may be completely incapacitating Patients with pulmonary emphysema are peculiarly subject to attacks of bronchitis and usually contract several such infections every winter Each attack leads to added damage to the lungs The infection itself favors further weakening of the pulmonary parenchyma and the swelling of the bronchial mucosa brings about increasing expiratory obstruction, which induces greater dilatation and breaking down of the alveoli of the lung Furthermore during such a bronchitic seizure the blood pressure in the pulmonary arterial tree is raised and the strain on the right ventricle is increased so that commonly heart failure occurs during such an episode Bronchopneumonia is a frequent sequel of such a bronchial infection and gives rise to fresh damage of both lung and heart and often causes death

Pneumothorax may occur when a large emphysematous

bleb ruptures usually during a coughing spell or following sudden physical exertion The symptoms and physical signs do not differ from those of pneumothorax encountered in younger individuals Usually with immobilization in bed the air in the pleural space is absorbed in two to four weeks and no permanent evil results follow Certain patients repeatedly have such attacks In other cases a valvelike action of the ruptured lung is established so that with each inspiration air enters the pleural space and cannot escape into the lungs with expiration So a tension pneumothorax is set up an increasing volume of air is pumped into the pleura the mediastinum is displaced to the healthy side and severe even dangerous respiratory distress may ensue In such cases it may be necessary to withdraw some air from the affected pleural space This is done by attaching a rubber tube to a chest aspiration needle The free end of the rubber tube is inserted into a jar of water and the needle is inserted into the pleural space Thus the escaping air is allowed to bubble up through the water In cases in which the air is not absorbed or in which it re accumulates it may be necessary to attempt to seal the hole in the lung This can sometimes be done by injecting 20 cc of 20 per cent glucose solution into the pleura that is distended with air The resulting reactive inflammation may close off the tear in the lung Such a procedure of course must be done with great care under aseptic precautions and the patient must be immobilized in bed lying on the affected side for several weeks

In certain cases of pulmonary emphysema individual emphysematous blebs may reach a huge size forming what are known as *air cysts* in the lung Such a cyst may displace a whole lobe of a lung It can be diagnosed only by the roentgen picture and is often mistaken for pneumothorax Air cysts give rise to no symptoms and are susceptible to no treat



Fig 18 —Pneumothorax complicating pulmonary emphysema. Note clear area delineated by arrows

ment Their recognition is important only from the point of view of differential diagnosis They may persist unchanged and roentgen pictures taken at long intervals may be identical

The heart Symptoms arising in the heart in patients with pulmonary emphysema are caused most frequently by associated coronary artery sclerosis or hypertension These symptoms do not differ from those in patients with uncomplicated heart disease except that the right ventricular strain caused by the pulmonary disease is more apt to lead to right heart failure In long standing cases of emphysema particularly when there is much fibrosis of the lungs and when there have been repeated bouts of pulmonary infection right heart failure eventually occurs In its earlier stages it is difficult to diagnose for both dyspnea and fullness of the neck veins may be due to the emphysema alone It is in such cases that measurement of the circulation time of the blood is of particular value If the circulation time from the arm to the tongue is normal that is less than 18 seconds then it may be inferred that the symptoms are due to the pulmonary lesion But if the circulation time is prolonged it is evident that myocardial failure has set in and is contributing to the symptomatology

When right heart failure occurs the heart dilates rather rapidly dyspnea and cyanosis become intense the neck veins and the liver become engorged and there may be edema of the legs The lungs may eventually become congested and pleural transudate may accumulate The prolonged and intense stasis in the peripheral circulation increases the work of the left ventricle until it too fails Figure 19 shows the chest x ray of a man aged 45 with advanced pulmonary emphysema whose heart was compensated The heart is not enlarged but the arch of the pulmonary artery on the left bor



FIG 19—Pulmonary emphysema with hypertrophy of the conus arteriosus and of the right ventricle of the heart



FIG 20—Same patient as in the preceding six months later Great cardiac dilatation accompanying heart failure

der of the heart is prominent suggesting dilatation of the pulmonary artery and hypertrophy of the right ventricle Figure 20 was taken exactly six months later when the patient had suddenly become gravely ill with severe heart failure that led to death within a few weeks Generalized cardiac enlargement is apparent Such a degree of cardiac dilatation rarely recedes Treatment of severe right heart failure in patients with pulmonary emphysema is exceedingly unsatisfactory Cardiac compensation usually cannot be restored and death follows within a few weeks or months

Hernias Hernias commonly develop in patients with emphysema and chronic bronchitis The cough by forcibly raising intra abdominal pressure gradually forces intra abdominal structures through points of weakness in the abdominal wall In older patients the giving way of the abdominal wall is favored by the increasing weakness and atrophy of the body musculature Usually one encounters inguinal and umbilical hernias In patients with operative scars ventral hernias commonly develop Operative treatment is uniformly unsuccessful for the persistent cough speedily leads to a recurrence of the hernia An appropriate truss should be provided

Treatment —No treatment can restore the emphysematous lung to normal but careful supervision and regulation of the patient s life can arrest the progress of the disease prolong life and postpone complications The two elements that favor progression of the lesion are pulmonary infection and factors such as cough that tend to increase intrapulmonic pressure Cough is favored by bronchial infection, by exposure to dust and by smoking These patients must avoid dusty occupations such as that of a baker They should give up smoking completely Smoking harms patients with pulmonary disease infinitely more than it does those with angina pectoris Bron

chial asthma is a direct cause of many cases of pulmonary emphysema so that it is essential to try to prevent asthmatic seizures In older patients one rarely finds a specific allergen that is responsible for the asthmatic attacks There may be multiple sensitivities but in the majority of the older patients with well established involvement and emphysematous changes in the lungs we are dealing with an infectious asthma which is difficult to eradicate Treatment of sinus infection and removal of polyps rarely lead to permanent relief At times autogenous vaccines prepared from the patient s sputum are helpful

Prevention of recurrent attacks of bronchitis is more easily talked about than accomplished Of course the patient should avoid exposure to raw cold inclement weather and drafts When he is obliged to go out in rainy or cold weather he should protect himself against the elements He should avoid other persons who have colds or grip for bronchitis commonly follows an apparently mild coryza

The best measure one which unfortunately cannot be carried out by the majority of patients is removal to a warm equable climate Many of these patients do well in Florida or in southern California Others do better in the drier climate of New Mexico or Arizona The emphysematous patient does not tolerate the cold raw northern winters

Many patients with pulmonary emphysema obtain symptomatic relief by wearing an appropriate abdominal belt It will be recalled that in these patients the diaphragm is pushed down in the position of inspiration and that its respiratory movements are small The diaphragm can be pushed up toward its expiratory position by a properly adjusted abdominal belt From this position contraction again occurs

[2] Alexander H L and Kountz W B Symptomatic Relief of Emphysema by an Abdominal Belt Am J M Sc 187 687 May 1934

The patient experiences increased ease of respiration and the vital capacity of the lungs may increase by as much as 40 per cent

Regulation of the bowels is of particular importance in these patients because constipation makes them strain at stool, and this in turn raises the intrapulmonic pressure and so favors progression of the emphysematous process

Breathing exercises often bring about symptomatic improvement increase vital capacity and lessen dyspnea The exercises are directed to teaching the patient diaphragmatic breathing They are described in greater detail in the section on asthma (p 252)

Medication is not curative in pulmonary emphysema It is designed to give symptomatic relief from the cough When there is much wheezing due to bronchial spasm or congestion ephedrine hydrochloride ⅜ gr combined with phenobarbital ½ gr is often helpful This may be given from two to four times a day In the presence of hypertension or coronary disease it should be administered cautiously In my experience expectorants are of little value and too often they upset the stomach Small doses of potassium iodide 2 to 5 gr three times a day may be given When the cough is at all severe codeine is the only drug that will help The dose should be the smallest that will alleviate the cough It is best to try doses of ⅛ gr first and to give larger doses only if necessary Nothing will stop the characteristic morning cough by which the patient clears the lungs of the secretions accumulated during the night Their expulsion after all is necessary Atropine gives no relief and often aggravates the symptoms by causing dryness of the respiratory mucous membranes and inspissating the secretions

Any slight cold or upper respiratory infection should be treated as a serious complication, for in emphysematous pa

tients bronchitis or bronchopneumonia commonly follows The patient should be put to bed in a room of equable tem perature and free from drafts The diet should be light the bowels should be kept open If bronchitis occurs treatment with penicillin or sulfadiazine should be instituted at once It is impossible to distinguish between severe bronchitis and early bronchopneumonia in these patients and it is danger ous to await the development of frank signs of pneumonia Often a serious infection can thus be aborted If breathing is difficult steam inhalations may be grateful A sedative cough mixture such as Stokes expectorant should be given If necessary codeine may be added to it If there is much respiratory difficulty and especially if there is increasing cya nosis oxygen may give great relief This may be administered by nasal catheter or through a B L B mask Morphine should be avoided because it depresses respiration and favors accumulation of secretions in the lungs and development of bronchopneumonia With the onset of bronchitis digitalis should be given routinely The bronchitis places an additional strain on the right ventricle and may induce heart failure Digitalis may prevent this Further by improving the circu lation through the lung it hastens resorption of the inflam matory process It is best administered as the 1½ gr 1 cat unit tablet For one week two tablets a day should be given After the first week the dose should be reduced to one tablet a day In the presence of fever and dyspnea the patient should be kept quiet usually in bed but his position should frequently be changed and he should be encouraged to sit up in bed *Often he is more comfortable in an easy chair As soon as* possible when the temperature has subsided or when it does not exceed 100 F he should be up part of the day This pro motes deeper respiratory excursions and helps to clear the lungs Older patients are greatly prostrated following an at

tack of bronchitis and it may take weeks for them to recover their strength The effect of so called tonics is notoriously difficult to estimate but many patients are apparently helped during convalescence by taking 2 mg of thiamine hydrochloride and 50 mg of niacin three times a day At times strychnine sulfate 1/30 gr seems to improve their strength

Aerosol administration of penicillin may clear up bronchial infections A nebulizer like the DeVilbis No 40 filled with 200 000 units of penicillin in 2 cc of water is connected with a small oxygen tank equipped with a reducing valve There is a hole in the tubing proximal to the nebulizer The oxygen is turned on and the opening of the nebulizer placed in the mouth Inhaling the patient closes the hole with his finger exhaling he opens it and continues until the penicillin solution is exhausted This is repeated several times daily

If bronchopneumonia develops it is treated as any other bronchopneumonia (see p 389)

Severe *heart failure* complicating pulmonary emphysema is very grave The patient should be put at complete rest in bed His fluid intake should be limited to 1 000 cc in 24 hours If the neck veins are full and the liver is engorged and if the red blood cell count is high one or more phlebotomies of 500 cc give great relief Oxygen should be administered continuously until the heart failure is controlled Digitalis 1½ gr twice a day should be administered and continued at this dosage for at least two or three weeks If the patient has had no previous digitalis medication larger doses may be given the first day One may give an initial dose of 6 gr and a second dose of 6 gr six hours later If there is insufficient response to these measures a mercurial diuretic 2 cc of mercupurin should be given intravenously or intramuscularly This may be repeated as indicated every three to seven days Severe heart failure in patients with emphysema has a

poor prognosis Rarely is compensation fully restored Death commonly follows in weeks or months

Operation in an emphysematous patient is hazardous because of the danger of postoperative pneumonia Ether is best avoided as an anesthetic because of its irritation of the lungs Local anesthesia avertin gas oxygen cyclopropane and ethylene are the anesthetics of choice Use of plaster spicas that limit the movement of the chest or diaphragm is dangerous and should be avoided Such immobilization of the chest will almost certainly induce a bronchial infection

Pulmonary Fibrosis and Bronchiectasis

Pulmonary fibrosis is common in older individuals and is usually associated with emphysema It results from repeated pulmonary infections and is localized chiefly in the lower lobes When such fibrosis becomes more extensive bronchiectasis is found with it The typical bronchiectatic dilatations in older persons are usually not as great or as destructive as those found in younger individuals following suppurative or interstitial pneumonia In older persons repeated attacks of bronchitis and bronchopneumonia lead to peribronchial inflammation and fibrosis and weakening and dilatation of the bronchial wall

The disturbance of respiratory function and the symptoms resemble those of advanced pulmonary emphysema However cough productive of much sputum is one of the chief complaints The sputum is rarely foul and is not as copious as in younger persons with bronchiectasis The cough is most aggravated in the morning on arising and persists until the bronchi have been cleared of the nocturnal accumulation of secretions Incurvation of the finger nails or clubbing of the fingers is common These patients are particularly subject to

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acute reinfection of the lung With such reinfection there is fever the sputum becomes more purulent, and bronchopneumonia usually develops At times there is hemoptysis which arises from granulation tissue or from dilated venules in a dilated bronchus This too is not nearly as common in the type of bronchiectasis seen in elderly individuals It is always alarming to the patient rarely, it may be exsanguinating Aspiration of blood and secretions into other portions of the lung may induce widespread bronchopneumonia and pulmonary damage

The physical signs of pulmonary fibrosis and bronchiectasis may be minimal Because these changes usually occur in an emphysematous lung the distended hyperresonant lung obscures the signs ordinarily produced by these lesions Often the only objective evidence aside from the characteristic cough are persistent rales in *one* of the lower lobes of the lung Dullness may or may not be present If the lesion is extensive or if there is little pulmonary emphysema dullness diminished breath sounds and moist, sticky rales may be heard over a lower lobe

The roentgen examination too is often of little help The hyperaeration of the lungs obscures the fibrotic changes One may see nothing but a few fibrotic streaks radiating down to the bases If the process is far advanced or if there is little emphysema the affected lung fields may be dark and the fibrous strands and dilated bronchi may be visible In such cases the intercostal spaces are narrowed and the heart and mediastinum may be drawn over to the affected side The dilated bronchi can be visualized by instillation of lipiodol and subsequent roentgen examination This procedure in old persons may give rise to serious irritative reactions even to pulmonary edema and it is rarely necessary or advisable to carry it out Such localization of bronchiectasis is of value

only when indispensable to diagnosis or when operation is contemplated This is a rare contingency in elderly patients

A serious form of pulmonary fibrosis and bronchiectasis is encountered in patients who have had excessive roentgen irradiation of the thorax for malignant lesions [3] One encounters this clinical picture in women who have been irradiated for cancer of the breast and in patients who have received roentgen therapy for neoplasms of the lung or mediastinum Such lung damage is usually accompanied by cutaneous damage such as telangiectasis or atrophy and induration The earliest lesion is a pneumonitis which may be accompanied by persistent fever cough and chest pain Gradually pulmonary fibrosis bronchiectasis areas of atelectasis and emphysema develop Adhesions form between the diaphragm and the lung and between the two layers of the pleura The lung shrinks the mediastinum is drawn to the affected side As in the case of other chronic pulmonary lesions the pressure in the pulmonary artery becomes elevated and atherosclerosis of the pulmonary arteries hypertrophy of the right ventricle and eventually right heart failure occur It is important to guard against this postradiation pulmonary lesion in patients receiving radiation to the chest Commonly the lesion is misdiagnosed as a pulmonary metastasis or a recurrence of the neoplasm and roentgen irradiation is continued with further destruction of lung tissue

Treatment —The general treatment of these patients is identical with that of patients with pulmonary emphysema Radical treatment such as pneumonectomy which is suitable for certain cases in younger people is rarely indicated in these older patients The process is more diffuse and the operative risks are too great Pneumothorax can seldom be

[3] Freid J R and Goldberg H Post Irradiation Changes in Lungs and Thorax Am J Roentgenol 43 877 June 1940

carried out because of adhesions. Excessive secretion of sputum can often be controlled by sharply limiting the intake of fluids and salt as in cardiac edema. The diet should be salt poor and the fluid intake restricted to from 800 to 1,000 cc. in 24 hours. These measures should be carried out strictly during periods when the secretion is excessive. When the acute process subsides they may be somewhat relaxed. During an attack of acute pneumonitis the administration of penicillin or of sulfadiazine 1 Gm. every four hours often brings the acute infection under control. In nonfebrile patients with excessive secretion roentgen therapy in moderately large dosage to the chest is at times successful in drying up the secretion. An average total dose of 1,200 roentgens through each of the anterior, lateral and posterior fields is employed. Each treatment consists of 75 roentgens to two or three fields.[4] During this treatment there is often exacerbation of cough and expectoration and there may be fever. Hemoptysis may occur. Improvement is first noticeable after about three fourths of the treatments have been given and continues for some four months after the cessation of treatment. Roentgen therapy does not cure the bronchiectasis; it helps resolve the chronic inflammatory reaction in the bronchi and lessens the bronchial secretions and exudates.

Removal of the patient to a warm, dry climate is probably the most useful procedure for obtaining a comfortable existence.

LIPOID PNEUMONIA

Lipoid pneumonia caused by inhalation of unassimilable *oils is not uncommon in elderly debilitated* persons, particularly in those with difficulty in swallowing. In a recently

[4] Berck, M., and Harris, W.: Roentgen Therapy for Bronchiectasis, J. A. M. A. 108:517 (Feb. 13) 1937.

reported series of 41 cases that were studied at autopsy 24 were in persons over 60 years of age and 11 in persons between the ages of 50 and 59[5] Liquid petrolatum or mineral oil is the offending agent in most cases At times this is introduced into the body by nasal instillation more often as a result of oral administration Oil introduced into the pharynx may enter the trachea without provoking cough or other distressing symptoms This occurs with particular ease when there is some disturbance of the swallowing mechanism due to local disease or to generalized weakness or impaired consciousness Thus it is found commonly in feeble old or cachectic individuals Once the oil has passed the glottis it trickles by force of gravity to the basal portions of the lungs

The pathological picture is characterized in the early stages by pulmonary alveoli crowded with oil filled macrophages These phagocytes enter the lymphatics and alveolar septa and then disintegrate A secondary fibrous tissue proliferation with collections of giant cells about coalesced oil droplets follows The end picture resembles that of chronic interstitial pneumonitis The lesions vary in size from small nodules to large masses that may involve an entire lobe At times oil can be scraped from the surface of the lesion

Lipoid pneumonia is usually asymptomatic and is discovered unexpectedly on the roentgen film or at autopsy The patient may have a mild cough and there may be occasional bouts of low fever Some patients experience recurrent attacks of bronchopneumonia Physical signs are often lacking In more advanced cases there may be dullness bronchovesicular breathing and rales at one or both bases Clubbing of the fingers does not occur Rarely oil droplets can be identified in the sputum These are significant only if the patient

[5] Freiman D G Engelberg H and Merrit W H Oil Aspiration (Lipoid) Pneumonia in Adults Arch Int Med 66 11 July 1940

has taken no oil for some hours before the sputum is collected

The roentgen findings may suggest the correct diagnosis The markings in the lower lung fields are exaggerated With more advanced lesions there are linear or nodular infiltrations that may coalesce to form larger areas of consolidation These changes are usually found in regions close to the cardiac or the diaphragmatic shadows The roentgen picture may simulate bronchiectasis basal tuberculosis or a pulmonary neoplasm

The diagnosis of lipoid pneumonia should be entertained in the case of a patient exhibiting persistent basal infiltrations and few symptoms Inquiry should be made in all such cases regarding the use of mineral oil orally or intranasally If there has been some difficulty in swallowing the diagnosis is rendered all the more probable A certain diagnosis can be made only by discovering oil droplets in the sputum

Unless the lesion is extensive it causes few symptoms and does not shorten life The gravest danger is complicating bronchopneumonia The increasing frequency of lipoid pneumonia calls for caution in the administration of mineral oil to debilitated patients

Bronchial Asthma

Bronchial asthma should be distinguished from the wheezing of chronic bronchitis and emphysema and the cardiac asthma of acute left ventricular failure Asthmatic bronchitis is manifested by continuous cough and wheezing In addition to sibilant and sonorous rales throughout the lungs large moist rales are audible throughout both lower lobes Acute paroxysms of dyspnea are brought on by attempts to cough up the profuse viscid sputum or by bouts of acute reinfection of the bronchi Paroxysmal dyspnea due to acute left ventricular failure usually occurs at night It occurs only when

there is serious disease of the heart particularly hypertension or coronary artery disease associated with considerable enlargement of the left ventricle In the absence of cardiac enlargement paroxysmal dyspnea cannot be attributed to the heart Confirmatory signs of myocardial weakness must be present such as rapid heart rate feeble heart sounds gallop rhythm accentuation of the pulmonic second sound and pulsus alternans

True bronchial asthma induced by sensitivity to specific allergens becomes less common with advancing years An allergic asthmatic person who survives past middle life has developed multiple sensitivities his asthma is induced by a great variety of factors he has developed emphysema and bronchitis and he has become sensitive to the bacterial infection in the bronchial tree So with the years the clinical picture of his asthma gradually changes from intermittent attacks with intervals of well being to continuous milder respiratory distress and wheezing with exacerbations brought on usually by reinfection by catching cold or by an attack of *bronchitis*

The patient has the typical appearance of advanced pulmonary emphysema The chest is barrel shaped expiration is prolonged and the expiratory murmur is faint There is much cough with mucopurulent sputum and moist and wheezing rales are heard throughout the lungs

Commonly the sinuses are infected and there are nasal polyps The appearance is cyanotic the fingers are clubbed

Although in these older asthmatics it is unusual to discover the allergen removal of which will relieve the symptoms it is wise to test the patient s sensitivity for at times therapy is successful Bakers who are sensitive to flour and furriers who are sensitive to fur find great relief by changing their occupation Other specific allergens may be found Discovery of

eosinophils in the blood or in the sputum should encourage the search for a specific cause

Treatment —The general treatment of these patients is identical with that of patients with pulmonary emphysema and bronchitis If a specific factor inducing asthmatic attacks is discovered this should be removed from the patient s environment and if this is impossible attempts at desensitization should be made The upper respiratory tract should be carefully examined by an otolaryngologist Nasal polyps should be removed and adequate drainage of the sinuses instituted Radical sinus operations in my experience rarely improve or lessen the asthmatic seizures Clearing the nasal passages to allow free breathing is helpful

Treatment of the acute asthmatic attack does not differ from that used for younger individuals Adrenalin should be used with caution in patients who have, in addition hypertension and coronary artery disease A subcutaneous dose of from 3 to 5 minims is usually tolerated and if it gives rise to no untoward symptoms may be repeated freely Ephedrine too may induce unfavorable reactions in persons with cardiovascular disease so it should be prescribed with care Because it may cause sleeplessness and restlessness it is best combined with a barbiturate such as phenobarbital It may be given in doses of ⅜ gr of ephedrine hydrochloride with ¼ gr of phenobarbital three or four times a day Frequently adrenalin is efficacious when given by inhalation by means of an atomizer generating a very fine spray For this the 1 100 solution is used The patient inhales the vaporized solution as soon as he feels his chest tightening In this way more severe attacks may be averted and the use of hypodermic medication avoided Certain vaporizers on the market are electrically driven and equipped with a face mask and are very efficient Their use may arrest an asthmatic seizure

that has been resistant to all other therapy including the hypodermic use of adrenalin The intravenous administration of 0 5 Gm aminophylline in 10 cc of saline solution will often halt an asthmatic attack The injection should be given slowly else nausea vomiting twitching or even convulsions may occur Aminophylline suppositories of 0 5 Gm are almost as effectual Given on retiring they will often insure a night free from attacks Some patients derive relief from the old fashioned remedies—smoking cigarets or burning powders containing stramonium leaves or saltpeter When the asthmatic attack does not yield to any of these remedies and when a status asthmaticus has set in the inhalation of helium and oxygen may be life saving Because helium has a much lower density than nitrogen a mixture of 21 per cent oxygen and 79 per cent helium has one third the density of air and therefore requires much less effort to breathe than air and oxygen In obstructive dyspnea such as in asthma the use of such a helium oxygen mixture lessens the inspiratory effort and aids the ventilation of the lungs It is best administered through the B L B mask In all older patients with severe bronchial asthma it is wise to give digitalis to prevent right heart failure For one week the dose should be 3 gr daily and after this 1½ gr daily Medication should be continued as long as the asthmatic seizures persist Sedatives should be used with great caution Because of the patient s distress and restless ness there is always the temptation to give drugs that will quiet him and lessen his anxiety Yet there is considerable danger in their use because of their depressant action on the respiratory center Morphine the barbiturates chloral hydrate and paraldehyde may all cause respiratory arrest and death in patients in status asthmaticus Morphine is especially dangerous and should be avoided The other sedatives may be given cautiously in small doses Atropine not only

gives no relief but often makes matters worse by making the bronchial secretions still more viscid and difficult to expectorate

Between attacks, the treatment of these patients is identical with that of patients with pulmonary emphysema At times treatment with autogenous vaccines prepared from the patient's sputum lessens the frequency of asthmatic attacks

Respiratory exercises are very useful In asthmatic patients inspiration opens the bronchi and the prolonged active expiration compresses them As a result of long standing asthma the ribs remain in an elevated position and the chest muscles become shorter and remain in this state of contracture even after the acute asthmatic attack is over The altered position of the ribs enlarges the chest cavity and the lungs become overexpanded to fill the greater chest cavity Exercises are directed to reduce the chest cavity to normal size Ordinary breathing exercises are useless for they increase the expansion of the chest Exercises should be directed to teaching the patient to use the lower chest muscles and the diaphragm They should be given systematically and under expert guidance They should be carried out before a mirror and should be taken on arising in the morning and at night Once they have been learned they should be instituted when an asthmatic attack is impending If breathing is too asthmatic adrenalin or ephedrine should be administered before the exercises are begun The primary exercise consists of a quiet small nasal inspiration This should be accomplished by a contraction of the diaphragm not by an elevation of the upper part of the chest The patient should keep his hand on his epigastrium and with the descent of the diaphragm he will feel the upper abdominal wall bulge forward as it is displaced by the descending diaphragm Inspiration should be followed by prolonged expiration through the mouth The

patient s attention is concentrated on this act if he makes an F or S" sound with his mouth while exhaling Expiration should be accomplished by a contraction of the abdominal muscles and of the lower chest muscles and should be pro longed to the limit of the patient s capacity At the end of such an expiration the patient may hear wheezing at the bases of his lungs and may cough but the procedure should be persisted in With the next inspiration the abdominal muscles should again be allowed to swell out Complete relax ation is important At first the exercises should be taken very easily A session should last 10 minutes

When this elementary breathing has been learned a broad belt of cloth should be placed around the lower ribs and the free ends of the belt held in the patient s hands At the end of expiration he should tighten the belt to empty the lungs completely Still holding the belt tight he should inspire and through his inspiration expand the belt

When these exercises have been learned general calis thenics designed to strengthen the abdominal and back muscles should be added In carrying out such calisthenics careful attention should be paid to proper breathing during their execution [6]

PULMONARY TUBERCULOSIS

About 25 per cent of persons past the age of 50 have latent tuberculous foci Tuberculosis mortality in adults remains at a steady level up to age 60 after which there is a slow in crease The mortality rate for ages 50 to 59 is 62 per 100 000 for ages 60 to 69 it is 70 and after age 70 it is 75 per 100 000 After age 40 men are twice as commonly affected as women

[6] Asthma Research Council *Physical Exercises for Asthma* (3d ed London Kings College 1939)

The disease occurs with such frequency that physicians should search for it in all older patients with chronic pulmonary disorders

Tuberculosis in persons past the prime of life is rarely a fresh infection Almost invariably the disease was contracted in youth or in early adult life It may become reactivated at any age Such renewed progression of the disease is favored by intercurrent wasting diseases malnutrition unfavorable working and living conditions and alcoholism The tuberculin reaction is not a reliable guide to the presence of tuberculous infection in the aged One study revealed 36 per cent negative tuberculin reactions in persons past 65 who had definite roentgen evidence of pulmonary tuberculosis

Tuberculosis in the elderly usually takes the form of fibroid phthisis There is great connective tissue reaction the interlobar connective tissue proliferates the pleura becomes greatly thickened the bronchi become dilated and bronchiectatic Compensatory emphysema develops in the uninvolved portions of the lung When cavities occur they are very thick walled There may be marked retraction of the lung pulling the mediastinum and heart over to the affected side

In these cases the infection is an indolent one, there is little fever the temperature may be subnormal and there may be little cough and sputum but the pulse is apt to be rapid The chest resembles that in emphysema although there is usually retraction or flattening of the apices with wasting of the overlying musculature Displacement of the mediastinum to the side where the lung is most shrunken can be recognized by observing the position of the trachea and of the cardiac apex (Fig 22) The lungs are hyperresonant to

Amazon P "Tuberculin Reaction in Old Age" Am Rev Tuberc 47 11 January 1943



Fig 21 —Healed calcified pulmonary tuberculosis

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[7] Amazon P "Tuberculin Reaction in Old Age" Am Rev Tuberc 47 41 January 1943



Fig 22—Chronic fibroid phthisis Note fibrosis especially of the left upper lobe pulling the trachea and the mediastinum to the left

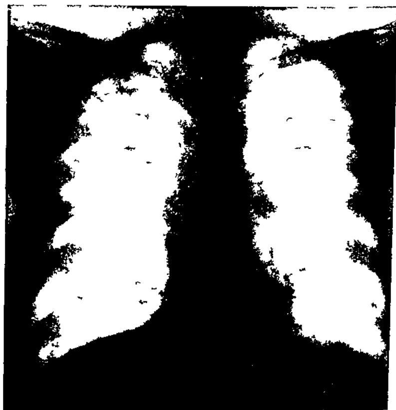


Fig 23 —Chronic fibroid phthisis and hypoplastic heart



Fig 24 —Same patient as in the preceding two years later Cardiac dilatation accompanying right heart failure

10 years after the discovery of their lesion Their distress from increasing respiratory difficulty and impaired pulmonary ventilation slowly progresses Hemoptysis occurs but is less common than in the caseating form of tuberculosis At times, rapid spread of the tuberculous lesion with caseation may occur As in other patients with pulmonary fibrosis and bronchiectasis right heart failure is common and may cause death Figures 23 and 24 are roentgenograms of a patient with chronic fibroid phthisis taken 24 months apart The dilatation of the heart was associated with heart failure Nontuberculous bronchopneumonia is often the cause of death Complications such as tuberculosis of the intestines and of the larynx so prevalent in fibrocaseous tuberculosis are rather infrequent

The fibrocaseous form of pulmonary tuberculosis constitutes nearly one half of all cases of pulmonary tuberculosis in adults over the age of 50 This has a rapid course as a rule and does not differ in its manifestations when it occurs in older individuals However a person with fibrocaseous pulmonary tuberculosis may live for three or more decades and the course of the disease may be marked by prolonged remissions and exacerbations Intestinal and laryngeal tuberculosis are common and death is usually due to the tuberculous infection

Diabetes mellitus and tuberculosis often coexist in older persons largely because of the increasing incidence of diabetes in the later periods of life The diabetes activates the tuberculous lesion and leads to its rapid progress unless the diabetes is strictly controlled

The association of asthma and pulmonary tuberculosis is frequent Harkavy found clinical and roentgen evidence of tuberculosis in 10 per cent of 400 cases of asthma studied in his clinic About half of these patients reacted to foreign

proteins of the inhalant group The other half had foci of infection in their respiratory tracts and behaved just like patients with asthmatic bronchitis who are free from pulmonary tuberculosis The association of tuberculosis and asthma therefore is accidental and not due to the tubercle bacillus

Treatment —The treatment of active caseous tuberculosis in older persons does not differ from that employed for younger individuals Because of the presence of extensive adhesions pneumothorax treatment is usually unsuccessful Radical thoracoplasty is less well borne in elderly persons and is rarely indicated Patients with chronic fibroid phthisis do not require intensive treatment It is most important to impress upon them that they have tuberculosis and that their sputum is full of tubercle bacilli that may infect others If they will learn proper personal hygiene many of these patients can stay at home Residence in a sanatorium or hospital is rarely advisable because specific treatment is useless and the disease lasts many years Only for the poor and homeless is institutional care indicated and these need some form of custodial rather than hospital care In general the treatment corresponds to that of patients with pulmonary emphysema and fibrosis The patient should avoid cold and exposure to inclement weather Residence in a warm climate is beneficial The patient should not overtax himself physically and should have plenty of rest Many can carry on a sedentary occupation The diet should be varied and plentiful and every effort should be made to maintain an optimum weight The patient should weigh himself at weekly intervals Symptomatic medication for the cough is often needed When the process is far advanced or when intercurrent nonspecific infections occur the physician should be on the watch for right heart failure and treat it as outlined in the section on pulmonary emphysema When there is associated diabetes

treatment of the metabolic disorder should be strictly followed Since it is essential to maintain the patient's weight it will usually be necessary to give insulin in addition to an appropriate diet

Tumors

Pulmonary neoplasms are being recognized with increasing frequency and there is evidence that there has been a definite increase in their incidence They occur for the most part in persons over the age of 50 so that in an aging population more cases will be encountered The onset of cough hemoptysis or pain in the chest in a person past middle age should always arouse the suspicion of carcinoma of the lung Men are affected far more often than women Physical signs are often scanty so that the diagnosis rests largely on roentgen examination and on bronchoscopy Both of these procedures should be promptly employed when a suspicion of pulmonary neoplasm exists Routine x ray may disclose a latent lesion

Benign tumors of the bronchus are uncommon They are met with in young and old Cough and hemoptysis are the leading symptoms The physical signs are those of atelectasis for the adenoma causes a partial obstruction of the bronchus with collapse of the pulmonary tissue behind the obstruction The physical signs are dullness and diminished breathing over the affected area When infection occurs behind the obstructing lesion fever and purulent sputum develop The roentgen film often does not reveal the lesion Extensive atelectasis or pneumonitis will show on the roentgen film Diagnosis is made by bronchoscopy The tumor usually can be removed through the bronchoscope followed by complete recession of symptoms and physical signs Delay may lead to pulmonary infection and secondary bronchiectasis

Malignant tumors of the lung are far more common than benign tumors The most frequent lesion is a neoplasm arising from one of the large bronchi These comprise fully three fourths of malignant pulmonary neoplasms These growths are highly invasive and extend into the lung and mediastinum There is early involvement of the hilar lymph nodes Metastases are common and occur with particular frequency in the liver brain and bones Cough and hemoptysis are early symptoms and result from ulceration of the tumor In these cases too atelectasis and infection of the lung behind the obstruction commonly occur The physical signs are dullness and diminished or absent breathing in the affected area The mediastinal structures may become involved There may be paralysis of a recurrent laryngeal nerve or invasion of the pericardium More commonly there is extension to the pleura with development of a pleural effusion When this occurs pain and tenderness of the chest wall are frequent The pleural fluid may be bloody Tumor cells discovered in the pleural fluid may reveal the diagnosis At times metastasis occurs to the lymph nodes at the root of the neck just behind the medial end of the clavicles Such nodes can be palpated by inserting the finger behind the episternal notch and the insertion of the sternocleidomastoid muscle Removal and histologic examination of such a node may clinch the diagnosis More rarely tumor cells may be found in the sputum The roentgen picture of these tumors depends on the presence or absence of stenosis of a bronchus In the case of a stenosing tumor there is atelectasis In the absence of atelectasis infiltrating shadows may be seen at the root of the lung extending out toward the periphery Enlarged mediastinal nodes are often seen In this type of lung tumor bronchoscopy almost always reveals the lesion and histologic examination of a removed specimen discloses its nature Bronchos

copy should be carried out freely if there is valid reason to suspect a pulmonary neoplasm

In the early stages the symptoms are not very striking—chiefly cough and pain in the chest There is little or no loss of weight and no anemia There may be clubbing of the fingers Any unilateral pulmonary lesion in an older person should arouse the suspicion of malignancy Because of the frequency of secondary infection a lung tumor may masquerade as a lung abscess or as indolent bronchopneumonia A carcinoma may develop in an old tuberculous cavity

One quarter of all lung tumors are what Rabin has called the circumscribed type They occupy the parenchymal and peripheral zones of the lung and arise from the smaller bronchi These tumors grow slowly and metastasize late For a long time there may be no involvement of the mediastinal lymph nodes The tumors may long remain silent and give rise to no symptoms Extension to the pleura and overlying structures eventually causes localized pain and tenderness Cough is insignificant Clubbing of the fingers occurs early Roentgen examination reveals anywhere in the lung fields a discrete circular shadow These tumors occur in regions inaccessible to the bronchoscope and so can rarely be visualized by its use

Treatment —Roentgen treatment is ineffectual and it is rarely worth while subjecting the patient to the expense and discomfort of this procedure The only hope of cure lies in operation With the discrete peripheral tumors operative shock is not great and even older persons have a good chance of withstanding the procedure Since operative removal offers the only hope it should always be undertaken Before submitting the patient to operation every effort should be made to determine whether there are any metastases which would render the operation futile In particular the spine and the



Fig 25 —Primary carcinoma of the lung

long bones should be x rayed for they are favorite sites of metastasis In the case of the more diffuse tumors, operation is much more formidable and is rarely successful in eradicating all of the tumor tissue Usually the whole lung and the mediastinal glands at the root must be removed The operative mortality is great Patients over the age of 60 can hardly stand such a procedure

Neoplastic involvement of the pleura is usually secondary to a growth in the lung or adjacent structures It results in rapid accumulation of fluid which is apt to fill the whole pleura and cause intense dyspnea The fluid is often bloody When removed by paracentesis it rapidly reaccumulates Diagnosis of the nature of the lesion can be made by examination of the pleural fluid The fluid is centrifuged and the sediment imbedded in paraffin and sectioned and stained for microscopic study Roentgen examination of the chest immediately after removal of the fluid may reveal lesions of the lung or pleura Treatment is ineffectual Chief reliance must be placed on codeine and morphine Fluid should be removed whenever it is necessary to relieve dyspnea

Secondary or metastatic tumor deposits in the lung are common They are seen particularly in patients with hypernephroma or with cancer of the breast prostate or thyroid They are usually discovered by routine roentgen examination for until the late stages they give rise to no physical signs Their metastatic nature is revealed by the fact that they are multiple and diffusely scattered throughout both lung fields

Lung Abscess

Lung abscess is not peculiar to older persons and its course *in the elderly has no unusual features* Lung abscess is of bronchogenic origin due to aspiration of infected material

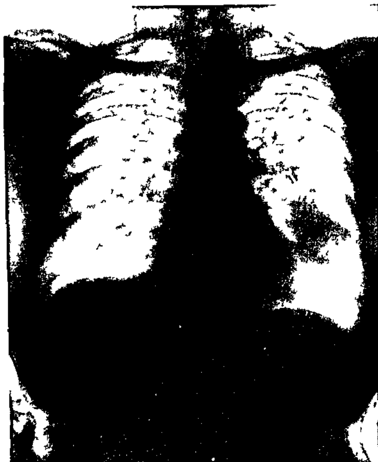


FIG 26 —Solitary metastasis to the lung from a hypernephroma

The infection is usually an anaerobic one, giving rise to a putrid abscess *The source of the infective material is usually the mouth* aspiration commonly following operations on the mouth or tooth extractions Pyorrhea is common in older persons Aspiration of the highly infective pus readily occurs during anesthesia for operations that do not involve the mouth *It is important therefore to have the patient's mouth put in good condition before subjecting him to any operation*

The pathological lesion is a necrotizing inflammation of the affected bronchus and adjacent bronchioles which soon involves the surrounding lung tissue Reactive localized pleurisy always occurs Breakdown of the gangrenous infected area quickly takes place and the softened material is coughed up

Symptoms —Three to five days elapse between the aspiration of infected matter and the first clinical manifestations The first symptoms are fever and chilliness Sharply localized pain in the chest due to pleuritic involvement soon follows The site of the pain marks the location of the abscess Subsequently cough develops and sooner or later usually in two weeks *foul sputum is coughed up Even before* this a foul odor may be observed on the breath particularly if one smells the patient's breath immediately at the end of a coughing seizure Recognition of this odor is most important for it is a pathognomonic sign Hemoptysis is invariably *present Physical signs are usually absent* At most there may be a small area of dullness and diminished breathing Localized tenderness of the chest wall over the abscess is an important sign Roentgen examination may at first show nothing but a circumscribed area of infiltration but within two or *three weeks a cavity with a fluid level will be evident* Bronchoscopy will reveal the precise origin of the pus and will help localize the lesion In many cases bronchography with iodized oil is necessary for exact localization

Treatment —Spontaneous cure occurs with sufficient frequency to warrant initial expectant treatment But the patient should be kept under close observation and there should be repeated roentgen examination If in the course of three or four weeks the fever subsides the sputum becomes scanty and the lesion on the roentgen film smaller one may await a spontaneous cure If cough and fever persist and if the roentgen film shows an extension of the lesion operative intervention is indicated indeed it may become an urgent procedure In former years delay in operation was the rule The result was development of chronic lung abscess with widespread pulmonary involvement multiple cavities and bronchiectases At such a stage medical treatment is ineffectual and operative intervention which usually calls for lobectomy or pneumonectomy is exceedingly hazardous Operation on an acute lung abscess involves relatively slight risk and gives gratifying results The most important measure preceding operation is accurate localization of the abscess because if the incision is not made directly over the abscess where the two layers of the pleura have become adherent putrid empyema may result Both the localization and the surgical treatment of pulmonary abscess represent highly specialized technics and should be entrusted to physicians with special training

Chapter Eleven

DISEASES OF THE GASTRO INTESTINAL TRACT

GASTRO INTESTINAL disturbances are among the most frequent causes that impel old people to seek medical aid In half of these cases there is a disorder of function without the presence of organic disease There are no gastro intestinal disorders that are confined exclusively to aging persons but bodily changes that come with aging impress a certain pattern on some of these diseases

Gastric acidity gradually declines with advancing years Although approximately one half of all persons over the age of 60 have normal or high gastric acidity many show diminished secretion and about one third have no free hydrochloric acid Histamine stimulation will produce acid secretion in about one half of those with anacidity Pepsin secretion is depressed but not lost in these cases Atrophy of the papillae of the tongue and secondary anemia often accompany the achlorhydria The emptying time of the stomach does not change with age

The salivary enzymes are diminished in amount so that the first stage of starch digestion is greatly depressed However pancreatic amylase is present in sufficient quantity that old people do not suffer from incomplete carbohydrate digestion There is some diminution in trypsin and lipase secretion by the pancreas

Loss of appetite may be related to a lessening of the senses of taste and smell and possibly to diminished hunger contractions due to gastric atony Up to a certain point it may be a useful adaptation that reduces the food intake when the energy requirements of the aging body diminish The stomach and intestines of aging persons like their hearts lack reserve power so that large meals cannot be taken without distress The power of digestion in the aged is markedly influenced by fatigue When old people are tired they lose their appetites or if they do eat they develop digestive upsets

The general dietary management of the aged has been discussed in Chapter 3

Constipation

Constipation is one of the commonest complaints of older persons There are a number of causes of constipation and treatment should be based on recognition of the cause Constipation may be due to inadequate food intake or to a dry diet with scanty ingestion of fluids It may result from psychic disturbances or from bad habits It is the old story applying to young and old that regular evacuation of the bowels requires an unhurried regularity of defecation Often inconveniences in housing or in the mode of living are responsible for the establishment of improper bowel habits

Atonic constipation is due to loss of tone of the colon and of the abdominal muscles This may result from physical inactivity from general enfeeblement or from long continued use of cathartics and enemas Spastic constipation is due to an irritable spastic colon which breaks the fecal mass into many small segments and which by its spasm prevents the normal progress of the fecal column The descending colon is the chief site of this spastic process This type of constipation

is commonly associated with abdominal cramps, or peristaltic unrest The stool is hard and lumpy and broken up into many small fecal masses By abdominal examination one can often roll the tight sigmoid under the fingers as a thin cord Spastic constipation results from disturbed innervation of the colon This may be due to psychogenic factors to worry and overwork to excessive smoking or to drinking too much coffee Anal fissures or painful hemorrhoids may be responsible By dyschesia is meant that form of constipation in which the rectum fails to empty itself It is the end result of habitual neglect of the call to defecation The rectum and lower colon gradually become more and more distended the musculature gradually loses its tone and contractility In time the weakened muscular wall of the rectum is incompetent to expel the contents of its overdistended cavity Although the rectum remains overdistended with feces a passage may be opened through the center of the fecal mass and occasional watery movements may be evacuated

Before initiating treatment the physician should make sure that there is no underlying organic disease The sudden appearance of constipation in an older person should always be regarded with suspicion for it may be the first sign of a colonic neoplasm Inadequate food absorption due to obstruction of the cardia or the pylorus may give rise to constipation The occurrence of new growths of the gastro intestinal tract is so common in older persons that a careful roentgen study of the gastro intestinal tract should be made when there is the slightest doubt about the diagnosis

Treatment —First attention should be given to providing a well balanced diet regular hours for meals a regular hour for going to the toilet and adequate fluid intake A glass of water taken on arising is often helpful Withholding of all cathartics is essential to a cure of constipation When ca

thartics are withdrawn from a patient who has been depend ent on them for years several days or a week may pass before there is a spontaneous bowel movement This is a trying period for the patient who has become mentally conditioned to the supposed need for a daily evacuation The physician should explain to him that this delay can cause no ill effects and that the fear of auto intoxication from the retained stool can be dismissed as unfounded With patience and institution of appropriate treatment spontaneous evacuation of the stool will take place sooner or later Only in the very old or in feeble chair ridden or bedridden invalids should continuous reliance be placed on cathartics Such persons lack the strength and vitality to re establish normal bowel habits

In atonic constipation the roughage in the diet should be increased by giving plenty of fruits vegetables and salads Agar with or without mineral oil or psyllium seeds add bulk to the stool and are helpful

The regulation of spastic constipation calls first for an adjustment of the patient s mode of living He should avoid rush and hurry an attempt should be made to relieve him of anxieties He should adopt regular eating habits and should get sufficient sleep Radical reduction in the amount of coffee taken and in the amount of smoking is essential Min eral oil alone or with agar is useful Antispasmodics such as tincture of belladonna or atropine should be given almost to the point of tolerance that is just short of the dose that will produce dryness of the mouth or visual disturbances Fifteen *to 20 drops of tincture of belladonna or 1/150* gr of atropine sulfate three or four times a day is usually sufficient Syntro pan and trasentin which come in 50 mg tablets act like atro pine but are less apt to cause dryness of the mouth One or 2 tablets may be given three times a day It is well to add a mild sedative such as ¼ gr of phenobarbital to each dose of the

antispasmodic Chloral hydrate 5 gr with sodium bromide 10 gr in an appropriate vehicle makes a satisfactory sedative for these patients The amount of coarse vegetables raw fruits and salads in the diet should be reduced

When the rectum is overfilled with feces that cannot be evacuated they should be removed by the gloved finger Retention oil enemas may serve to soften the fecal mass Once the impacted mass has been evacuated the rectum should be kept empty with small enemas or glycerin suppositories

At times in old and enfeebled persons scybalous masses may cause intestinal obstruction Such scybala may be in the transverse or descending colon and may be felt on abdominal examination as firm masses giving rise to the suspicion of neoplasm At times there may be a small passage through the hardened fecal mass and alternating symptoms of constipation and diarrhea may further simulate carcinoma of the colon The history of the case a carefully given barium enema and a sigmoidoscopic examination may clear up the diagnosis Scybala should be softened by retention enemas of olive oil following which attempts should be made to dislodge them with soapsuds enemas and gentle massage

Peptic Ulcer

Peptic ulcer duodenal or gastric is a disease of youth and middle age Eusterman and Balfour report that about 8 per cent of patients with duodenal ulcer and 22 per cent of those with gastric ulcer are over age 50 at the first onset of symptoms Acute peptic ulcers with perforation or hemorrhage may occur in the aged The death rate from peptic ulcer especially from gastric ulcer increases progressively up to age 75 This is because older persons are less able to with

stand the complications that arise Mulsow[1] reports that 10 5 per cent of 4 079 published cases of peptic ulcer were in patients over 60 and that one third of all deaths from peptic ulcer occur after 60 A person who has once had a peptic ulcer is rarely cured the ulcer may heal and there may be a remission of symptoms but recurrences are the rule If such individuals with recurring ulcers survive to advanced ages they may still exhibit ulcer symptoms Peptic ulcer occurs more often in males than in females Although the etiology of peptic ulcer remains obscure it seems probable that in persons over the age of 60 arteriosclerosis of the gastric and duodenal arteries is an important contributing factor This may account for the more continuous and chronic course of ulcers in the aged

It is unnecessary to enter into a detailed discussion of the symptomatology and treatment of peptic ulcer This can be found in any textbook of medicine I wish to discuss only the features of peptic ulcer that are distinctive of the disease as it manifests itself in older persons

Of first importance is diagnosis No matter how typical the symptoms no matter whether or not there is free acid in the gastric contents painstaking and expert roentgen study of the gastro intestinal tract must always be carried out Carcinoma of the stomach is so common in older persons and masquerades under such deceptive guises that it becomes the first duty of the physician to exclude it as a cause of the symptoms At times even the roentgen picture does not conclusively distinguish between cancer and benign ulcer of the stomach In persons past 50 malignancy should be suspected and operation undertaken if the ulcer is of short duration if it is more than 2 5 cm in diameter if it is in the prepyloric

[1] Mulsow F W Peptic Ulcer of the Aged Am J Digest Dis 8 112 April 1941

region or on the greater curvature or if there is gastric anacidity Ulcers rarely undergo malignant metaplasia so that an ulcer of known long duration may be regarded as benign

The classic symptom of peptic ulcer is epigastric pain occurring one or two hours after meals and relieved by food and alkalis Characteristic is a periodicity of the symptoms with long free intervals during which the patient feels well In the aged this periodicity is less evident the ulcer persists without healing and the symptoms become continuous Thus an older person who for decades has had ulcer symptoms every few years complains that the intervals of freedom from pain are becoming less and less and finally that the dyspepsia has become persistent Cases that have their onset after the *fifth decade may commence with the typical ulcer symptomatology* but again there is a tendency for the symptoms to continue despite treatment Night pain awakening the patient from sleep is characteristic of peptic ulcer and always indicates an organic lesion

Hemorrhage may occur as the initial symptom in older patients or it may develop during the course of the disease It may be manifested by hematemesis by tarry stools or by both In the absence of vomiting the patient may complain only of sudden weakness vertigo and palpitation or he may faint Often the true cause is overlooked and it is assumed that there has been some kind of heart attack Such symptoms invariably call for examination of the stool and estimation of the hemoglobin content of the blood Always a grave complication *hemorrhage is of especially serious import in older* persons in whom bleeding is apt to be intractable Ninety per cent of deaths from bleeding ulcer occur in persons over the age of 50 Three quarters of all deaths occur following the first hemorrhage At autopsy one finds a rigid calcified artery at the base of the ulcer with a wide open hole in its wall

through which the blood escaped It is no wonder that such a defect in a stiff unyielding thickened artery does not heal and does not give the blood an opportunity to clot As a result of serious hemorrhage and consequent shock coronary in sufficiency and cardiac infarction may occur in these older patients who in addition often have sclerotic coronary arteries

Perforation occurs less commonly in older persons with peptic ulcer than it does in the young

Except during periods of active bleeding occult blood is rarely found in the stools of patients with peptic ulcer Its discovery in older patients should always arouse the suspicion of gastro intestinal neoplasm Following hematemesis or melena the urea nitrogen of the blood may rise to a level of about 50 mg per cent This occurs particularly in older patients with renal impairment If the bleeding stops the blood urea drops to normal in a few days If the blood urea figure remains high it is an indication of continued bleeding

The association of coronary artery disease and ulcer in the same person is common This may cause difficulty in diag nosis for in such cases the patterns of pain of angina pectoris and of peptic ulcer may become interwoven Frequently the patient will complain of precordial pain radiating down the left arm coming on one hour after meals and relieved by food or he may experience epigastric pain on effort The mode of onset and the manner of relief of pain will reveal whether it arises in the heart or in the stomach

Treatment —Since peptic ulcer is a chronic recurring con dition and since symptoms are activated by indiscretions in diet and by mental and emotional strain the physician should direct his first efforts to regulation of the patient s life Dietary care must be more continuous than in the young because of the great tendency to chronicity of peptic ulcer in older persons The patient should learn to live an equable life

free from overwork and anxiety Alcohol and coffee should be prohibited Smoking too should be interdicted for it has a definite effect in activating ulcer symptoms

When ulcer symptoms are acute the patient should be put to bed He should receive a strict Sippy diet i e a 3 oz mixture of equal parts of milk and cream every hour, day and night It is particularly important to continue the feedings during the night so that neutralization of gastric acidity may be continuous Within a few days soft boiled eggs and well cooked cereals may be added Further increases of diet are governed by the patient s symptoms When the pain does not yield to this regimen and when as happens commonly night pain persists use of the milk drip is helpful A Rehfuss tube is passed into the stomach and connected by a long tube to a gravity flask and a Murphy drip bulb is intercalated in the rubber tube below the flask The flask is filled with milk which is allowed to drip at a rate of 30 drops a minute The patient receives 3 qt of milk in 24 hours The drip treatment may be given continuously for several days or only at night If pain persists 5 Gm of bicarbonate of soda may be added to each quart of milk

Alkaline powders such as bicarbonate of soda or magnesium oxide are not used as freely as in former years In excess they may cause alkaline intoxication particularly in the elderly Tribasic calcium phosphate and tribasic magnesium phosphate are poorly absorbed and may be used in the form of a powder containing 15 gr of each Colloidal aluminum hydroxide a preparation such as amphojel serves as a useful drug to control gastric acidity One teaspoonful may be given from three to six times a day

When ulcer symptoms are less acute the patient need not remain in bed, and a soft bland diet, divided into six feedings spaced throughout the day may be prescribed with safety

Tincture of belladonna 15 to 25 minims three times a day or atropine sulfate 1/150 to 1/100 gr three times a day allays pylorospasm and relieves pain

Pyloric stenosis with gastric retention does not always call for operation It often yields to a strict medical regime such as outlined above As a result of lessening spasm and of absorption of inflammatory reaction around the ulcer the pylorus may again empty itself freely If there is much retention a lavage every night gives great relief and hastens the reestablishment of normal gastric emptying

Operation —Penetrating ulcers of the stomach in patients over 50 years of age that have lasted only a few weeks or months always call for operation because of the impossibility of accurately distinguishing by any clinical means between benign ulcer and cancer If the ulcer is known to have existed for a year or more it may be regarded as benign and may be treated medically Whether to employ medical or surgical treatment for peptic ulcer in older persons is a decision that is difficult to make On the one hand these ulcers do not respond well to medical therapy and are frequently chronic indurated and persistent and on the other hand the operative risk of gastric surgery is much greater in older persons Each case must be decided on its merits Ordinarily medical treatment is to be preferred but if the symptoms resist all treatment and the patient has become a chronic invalid operation is indicated Unrelieved pyloric stenosis is another indication for surgery The operation of choice is subtotal gastrectomy In skilled hands the operative mortality is not excessive and cures are usually permanent Simple gastro enterostomy is never indicated except for pyloric stenosis In all gastric surgery the skill and experience of the surgeon are of paramount importance Statistics show that the operative mortality of a surgeon who does only occa

sional gastric surgery is much greater than that of the surgeon in a large hospital who does many such operations every year

When there is hemorrhage the physician is faced with the choice of employing expectant treatment with the accompanying danger of exsanguination or operation with its attendant high mortality In patients past the age of 45, medical treatment of bleeding ulcer is attended by a mortality of some 20 per cent, in the case of severe hemorrhage of 30 per cent Yet operation even with the free use of transfusion takes a still higher toll—close to 45 per cent Every patient with a bleeding peptic ulcer should at once be admitted to a hospital where he can be closely observed His blood should be typed and appropriate donors should be available The hemoglobin and red blood cells should be checked It has been learned during recent years that complete starvation is no longer essential The patient may be given a first day Sippy diet In many instances the bleeding stops Repeated examination of the hemoglobin, of the blood urea and of the stool for gross or occult blood will reveal whether or not the bleeding has ceased Transfusion is unnecessary unless the hemoglobin content drops below 45 per cent The blood pressure should be measured several times a day A drop in systolic pressure to 90 is a danger sign and should lead to a painstaking inventory of the situation If bleeding continues or if there are repeated severe hemorrhages operation must be undertaken and it is best not to wait too long By repeated transfusions the patient s hemoglobin content should be brought to as high a figure as possible and a subtotal gastrectomy should be performed No problem in clinical medicine requires greater judgment than the treatment of a patient with severely bleeding peptic ulcer Too great delay before operation may be fatal, and unnecessary operation entails a grave risk

When bleeding has stopped iron should be administered This may be given as feosol 2 tablets three times a day

Perforation always calls for immediate operation

Arteriosclerosis of the Mesenteric Arteries

With advanced arteriosclerosis and narrowing of the mesenteric arteries there may be intermittent symptoms of abdominal pain and indigestion occurring particularly after meals Ortner called this condition intermittent angiosclerotic dyspragia of the intestines and pointed out the resemblance between the mechanism of this pain and that of intermittent claudication The condition is not common

Mesenteric thrombosis and embolism is not confined to elderly individuals Rarely does the atherosclerotic process alone progress to the point of occlusion of a mesenteric artery Infection or embolism usually plays a determining role

Cancer of the Stomach

One third of all cancers in men and one fifth in women arise in the stomach Cancer of the stomach occurs from three to four times as often in men as in women Nearly three quarters of all cases occur after the age of 50 and by far the largest number are seen between the ages of 50 and 70 However the age specific death rates continue to rise even after age 70 and the predominance in the preceding decades arises from the fact that there are more persons living in the younger age groups The largest number of deaths occurs between the ages of 55 and 65 and the average age at onset is 53 years

The growth is usually an adenocarcinoma It may have a fungating polypoid appearance or it may be an infiltrating

ulcerating lesion Again there may be a diffuse firm fibrous growth involving the wall of the stomach This occurs usually in the pyloric end of the stomach and gives rise to the so called leather bottle stomach

Because the symptoms are not characteristic the diagnosis is often overlooked or made only at a late date when the lesion is far advanced and inoperable Nearly one half of the cases of cancer of the stomach seen in large hospitals and clinics are inoperable when they first come under observation The patient complains of vague indigestion that has existed for several months or even years Half the patients have had symptoms for more than a year Epigastric pain is common and its appearance is unrelated to the ingestion of food The symptoms may be intermittent Anorexia loss of weight and weakness appear in all cases When the growth involves the pylorus vomiting may be the first manifestation when it obstructs the cardia there is difficulty in swallowing Gastric hemorrhage may be the first symptom Secondary anemia is the rule and in ulcerating carcinomas that do not obstruct the pylorus chiefly in tumors of the posterior wall of the stomach profound anemia may be the presenting sign An abdominal mass is palpable in the minority of cases The sedimentation rate of the red blood cells is usually rapid Fever and leukocytosis occur with some ulcerating lesions

About one third of the patients have pain typical of peptic ulcer which often yields temporarily to the usual forms of ulcer treatment Achlorhydria is found in 60 per cent of cases The absence of hydrochloric acid is less commonly encountered since we have learned to recognize earlier lesions by means of the roentgen ray The discovery of occult blood in the gastric contents or in the stool is of great diagnostic value With marked pyloric obstruction the gastric contents may be foul and they may contain fermented food

blood lactic acid and the Boas Oppler bacillus Occasionally there is macrocytic anemia indeed the association of pernicious anemia and gastric carcinoma is not uncommon (p 422) The discovery of a pernicious anemia blood picture should not lead to neglect of a careful roentgen study of the stomach Metastases occur chiefly in the regional lymph nodes the liver and the lungs At times they involve the so called Virchow nodes in the left supraclavicular fossa Biopsy of such a hard nodule may clarify the diagnosis A rectal examination should always be made for peritoneal metastases to the rectal culdesac are common

Roentgen examination is the most useful method of diagnosis The only hope of discovering cancer of the stomach in the early operable stages lies in subjecting to gastro intestinal roentgen study every patient past middle age who has indigestion that is not promptly and permanently relieved by appropriate treatment St John and his associates attempted to detect early unsuspected carcinoma of the stomach by routine fluoroscopic study of persons over 50 who had no digestive symptoms They examined 2 413 persons and found malignant gastric tumors in 3 an incidence of 1 24 per 1 000 Roentgen study of the stomach requires great experience and a refined technic including the demonstration of the mucosal pattern with a thin coating of barium suspension It cannot be left to the casual observer who studies but a few cases a year The differentiation of a benign ulcer from a neoplasm is difficult and even after the most expert preoperative study a cancer may be mistaken for an ulcer or vice versa A lesion near the pylorus or on the greater curvature or the posterior wall of the stomach is more likely to be malignant The size of the lesion is a further aid Those more than 2 5 cm in diameter are most often malignant A lesion interpreted as an ulcer should be kept under close



FIG 27 — Carcinoma of the stomach

observation for several months Under appropriate treatment the symptoms should disappear and there should be roentgenographic demonstration of complete healing within a month The patient should be re examined at monthly intervals for a time and the lesion must stay healed The persistence or recurrence of an acute ulcer warrants the presumptive diagnosis of carcinoma The roentgen film is not an infallible guide to the extent or the operability of the tumor Walters reports that in 20 per cent of cases which the roentgenologist reported as inoperable it was possible to do a gastric resection Growths of the cardia and posterior surface of the stomach are easily missed and if the symptoms suggest gastric neoplasm a negative roentgen report should not be accepted The roentgen study should be repeated and gastroscopic examination should be carried out

Gastroscopy may reveal a lesion not demonstrated by the roentgen ray and may distinguish between a benign and a malignant lesion

Surgery offers the only hope of cure and operation should be attempted if there is reasonable suspicion of malignancy if there is the slightest chance that gastric resection may be possible and if there are no demonstrable metastases At present the outlook for cure of the average patient with gastric cancer is still very dark In the country at large the diagnosis is often made too late and when operation is finally undertaken the immediate operative mortality is over 50 per cent In institutions where special attention is paid to this disease the figures are more hopeful From Mayo Clinic[2] has come a report on 10 890 cases Of these 43 per cent were manifestly inoperable and 57 per cent were explored In about one

[2] Walters W Gray H K and Priestley J T *Carcinoma and Other Malignant Lesions of the Stomach* (Philadelphia W B Saunders Company 1942)

half of those cases that were explored, or 25 per cent of the whole series partial gastric resection was done The operative mortality for the whole series of resections was 16 per cent but the death rate in more recent years is becoming lower The older the patient the greater the operative risk Of those who survived operation 29 per cent lived five or more years

The prognosis depends on the size of the lesion and on its accessibility as well as on the age of the patient and on his general condition Most patients with gastric carcinoma especially those with pyloric stenosis are dehydrated starved and anemic Careful preoperative treatment with intravenous solutions of glucose amino acids and saline transfusion and parenteral administration of vitamins is essential

Early diagnosis and successful treatment of cancer of the stomach depend primarily on the general practitioner By constantly keeping on the watch for gastric cancer in every case of indigestion in elderly persons he will discover an increasing number of cases in their earlier and operable stages Success too depends on the roentgenologist the gastroscopist and the surgeon specially trained and experienced to cope with the problems of this disease

When the lesion is inoperable symptomatic treatment often gives great temporary relief The diet should be bland but nutritious and concentrated In the presence of secondary anemia iron should be given It is not uncommon to observe the hemoglobin level rise from 50 to 75 per cent and for the patient to gain weight under such treatment If there is much pain appropriate opiates should be given Radiotherapy is of no avail Palliative operations such as gastroenterostomy are rarely indicated, for they do not prolong life or give much relief

Cancer of the Lip

Cancer of the lip is usually a squamous cell carcinoma and involves the lower lip in 95 per cent of cases All but 5 per cent of cases are found in males and the average age of occurrence is 56 years The growth appears as an indurated plaque or ulcer Metastasis to the neck glands takes place very late Diagnosis rests on biopsy and tissue examination of every suspicious lesion Radiotherapy offers the best form of treatment for small growths and cures can be achieved in 90 per cent In the more advanced cases surgery may be necessary Dissection of the neck glands should be under taken only if there are palpable nodes

Cancer of the Tongue

Cancer of the tongue is the most malignant neoplasm in volving the region of the mouth Over 85 per cent of its vic tims are men Antecedent syphilis with resulting glossitis and a positive Wassermann reaction are found in almost one third of the cases In other instances the carcinoma may develop from leukoplakia Excessive smoking poor oral hygiene and ragged broken stumps of teeth are supposed to be predis posing factors It has been suggested that vitamin B defi ciency with its resulting lesions of the tongue and mouth is a common predisposing cause for oral carcinoma[3] The cachexia and mental depression of these patients are in part attributed to this deficiency which is progressively accentu ated by the difficulty in eating that results from the mouth lesions The neoplasm presents itself as an indurated pain less ulcer which in the later stages may become infected

[3] Hayes M and Koop C E The Precancerous Mouth Lesions of Avitaminosis B Am J Surg 57 195 1942

Metastasis occurs to the deep lymph nodes of the neck Again diagnosis rests on histologic examination of a removed specimen There is no stereotyped form of treatment Early lesions may respond to radiotherapy alone Commonly, a combination of surgery and radiotherapy is indicated Dissection of the cervical lymph nodes which is a formidable procedure should be undertaken when they are manifestly involved In the best clinics five year cures are reported in about one quarter of cases treated The associated stomatitis should be treated with large doses of vitamin B complex and a varied high caloric diet Vitamin B is best given in the form of granular dried yeast 1 tablespoonful two or three times a day, or else 6 ordinary yeast cakes may be taken daily Relief of the associated stomatitis gain in weight and lessening of nervousness and mental depression usually result

CANCER OF THE ESOPHAGUS

Cancer of the esophagus occurs most frequently in persons between 60 and 65 It is 10 times as frequent in men as in women It is situated most often in the upper third of the esophagus but may occur at any site The tumor causes stenosis of the esophagus The lesion may ulcerate and may perforate into the mediastinum lungs or pericardium leading to fatal infection

The earliest symptom is difficulty in swallowing solid food The patient feels the food bolus as it becomes lodged at the site of the lesion and swallowing may become painful Gradually the dysphagia increases and finally even soft foods and liquids will not go down At this stage there is frequent regurgitation of liquids Progressive and marked loss in weight results from lack of nourishment Fortunately there is an accompanying loss of appetite so that the patient does



FIG 28 —Pneumopericardium caused by perforation of cancer of the esophagus

not suffer from hunger Serious hemorrhage may occur Extension of the growth may involve the recurrent laryngeal nerves giving rise to hoarseness Pain in the chest may occur and always indicates extension of the growth to the surrounding structures There may be metastatic enlargement of the supraclavicular lymph nodes more often on the left Biopsy of such a node may confirm the diagnosis The patient becomes dehydrated but anemia is not very striking Carcinoma of the cardiac end of the stomach may simulate the dysphagia of cancer of the esophagus but the gastric localization leads to a more profound anemia Eventually the patient dies of starvation if perforation does not hasten the end

Treatment —Although the risk is great and the results are none too good operation should be attempted if the lesion is an early one without invasion of the mediastinal structures More and more instances of successful removal of esophageal carcinomas with construction of an artificial tube between the gullet and the stomach are being reported Radiotherapy is of no value If radical operation is impossible gastrostomy may keep the patient from starving Since this procedure carries with it a high mortality gives little comfort and does not prolong life appreciably, it should rarely be done

Cardiospasm

Cardiospasm is unusual at advanced ages although 10 per cent of all cases of this condition are described in patients over the age of 50 Cardiospasm usually begins in early adult life, but the condition may last for years Sturtevant[4] reports that of 189 cases 34 lasted over 10 years The longest reported duration of cardiospasm is 52 years Treatment is the

[4] Sturtevant M "Cardiospasm with Review of the Literature" Arch Int Med 51 714 May 1933

same as that in younger persons passage of appropriate sounds to dilate the cardia and psychotherapy

Diverticula of the Esophagus

Diverticula of the esophagus occur predominantly after the age of 50 *Traction diverticula* are found chiefly in the thoracic portion of the esophagus They arise from the con traction of inflammatory adhesions between the esophagus and surrounding structures Tuberculous lymph nodes are a common cause The apex of the diverticulum is usually directed upward so that little food enters it and no stasis occurs Therefore they rarely give rise to symptoms and are usually an accidental finding in the course of roentgen examination

Pulsion diverticula represent in essence a herniation of the esophagus through the middle or inferior constrictor muscles of the pharynx probably determined by a congenital weak ness of these structures The pouch gradually enlarges and as a rule extends to the left and may give rise to a bulge in the supraclavicular region The diverticulum may extend down ward into the thorax As the pouch enlarges and becomes distended with food it presses on the esophagus or angulates it and causes stenosis and dysphagia This favors increased filling of the diverticulum and a vicious circle is established Gradual loss of weight is the rule The earliest symptom is a peculiar sensation in the throat Gradually dysphagia develops Food stagnates in the pouch and may cause a foul odor of the breath There is frequent regurgitation of food as the pouch empties itself Commonly this occurs at night and may seriously disturb sleep Some of the regurgitated material enters the larynx and provokes severe coughing spells Bronchitis commonly follows and pulmonary suppura tion is a frequent complication Often such a diverticulum

can be recognized by having the patient swallow some water and then expressing the contents of the sac by pressure over it in the neck. A gurgling sound is then heard due to the escape of water and air from the pouch. Positive diagnosis is made by roentgen examination. Operative removal of the diverticulum offers the only hope of cure.

Diverticulosis and Diverticulitis of the Colon

Diverticula of the colon are herniations of the mucous membrane through gaps in the muscular coat of the large intestine. They may occur in any portion of the colon but 90 per cent of them are found either only in the sigmoid or else in the sigmoid with associated involvement of other portions of the colon. They develop in two rows just to the mesenteric side of the anterior and posterolateral taeniae coli at the points where the blood vessels penetrate the muscular coat. These are apparently weak spots in the wall of the gut. The appendices epiploicae are situated in the same areas so that diverticula are often covered and hidden by fat. The herniation of the mucous membrane through these susceptible regions is brought about by increased pressure within the bowel and this in turn results from prolonged and repeated spasm of the colon. Spasm, not atrophy or atony of the colon, is found associated with diverticulosis.

The condition of a colon with multiple diverticula is called diverticulosis. When these outpouchings become inflamed we speak of diverticulitis. From autopsy studies it appears that about 4 per cent of persons over age 40 have diverticulosis.[5] The condition is uncommon in younger age groups but increases in frequency with each decade. It is found at an

[5] Kocour, E. J. "Diverticulosis of the Colon." Am. J. Surg. 37: 433, September 1937.

topsy in 6 5 per cent of persons between the ages of 61 and 70 and in 8 per cent of those over 70 Two thirds of all cases occur in persons over the age of 60 Men and women are affected with equal frequency but diverticulitis inflammation of the diverticula is three times as common in men as in women The incidence of diverticulosis determined by roentgen studies is much higher Edwards[6] for instance reports that 16 per cent of persons over 35 years of age who had roentgen examinations by means of a barium enema had diverticula Such a series represents a selected group with gastro intestinal complaints and this accounts for the higher incidence

Diverticulosis gives rise to no symptoms but spastic constipation with vague abdominal discomfort is often encountered in patients with diverticula It is more likely that the spasticity of the bowel is the cause of the diverticula than that the diverticula cause the spasticity of the gut Diagnosis rests exclusively on roentgen examination preferably by means of the barium enema The earliest indications of diverticulosis are found in an irregularity of the indentations separating the haustra and an irregularity in the shape of the haustra As the condition becomes more advanced a part of the colon may exhibit a serrated border like a saw edge and here and there small outpouchings may be seen Fully developed diverticula appear as flask or club shaped protrusions along the wall of the colon usually the sigmoid Commonly they are seen better in the oblique than in the anteroposterior position

No treatment of the diverticula as such is possible but the spastic constipation should be combated because it presumably promotes the growth of diverticula and because fecaliths

[6] Edward H C *Diverticula and Diverticulitis of the Intestine* (Bristol J In Wright & Sons Ltd 1939)



Fig 29 —Diverticulosis of the colon

retained in the diverticula favor the development of diverticulitis The best measures are a low residue diet mineral oil and the use of atropine or one of the other antispasmodics

Diverticulitis occurs when a diverticulum becomes inflamed Fecaliths commonly collect in the diverticula Once they are formed they cannot escape because the diverticulum has no contractile power and its mouth is narrow Their presence favors the development of local infection and ulceration One eventuality resulting from diverticulitis is acute perforation with generalized peritonitis This is not very common and calls for immediate surgical intervention More often the inflammatory process is subacute and results in pericolitis Adhesions form and if perforation occurs a localized abscess develops The inflamed sigmoid may become adherent to adjacent structures particularly to the bladder A pericolic abscess may rupture into the bladder into another loop of the gut or into the free peritoneal cavity If the pericolic inflammation is extensive and of long duration the colon may become obstructed

The symptoms are varied With uncomplicated diverticulitis the patient complains of pain in the left lower quadrant and constipation or irregularity of bowel function There may be slight fever In mild cases the symptoms subside within a week or two Recurrent bouts of inflammation are common If pericolic abscess forms the symptoms are more persistent and there may be rigidity of the abdominal wall or a mass may become palpable If the inflammation involves the bladder there is frequent and painful urination If a colovesical fistula forms air and feces are found in the urine Sometimes inflammatory signs are in the background and the symptoms are chiefly those of intestinal obstruction A mass may be palpable in the left lower quadrant and carcinoma of the colon may be suspected

Treatment —Diverticulitis often subsides under conservative treatment The patient is put to bed given a liquid diet and an ice bag on the abdomen No cathartics or enemas should be administered If no signs of spreading peritonitis appear and there is little toxemia it is safe to await spontaneous recession If fever and tenderness persist if there is much peritoneal reaction if a mass becomes palpable or if there is intestinal obstruction or bladder involvement operation may become necessary Operation in these cases is a rather formidable procedure In all cases a permanent colostomy must be formed above the inflamed area of intestine If there is a perforation an attempt may be made to sew it up Usually this is impossible and then the omentum is wrapped around the inflamed area If there is an abscess it is best just to institute drainage without further manipulation for fear of spreading the infection When there is much inflammation or obstruction a colostomy is done and the bowel is exteriorized on the abdominal wall In the course of time the inflammation subsides and it may be possible to drop the bowel back The colostomy must be kept open for at least a year in these cases For indications for resection and for details of surgical procedure reference should be had to special treatises

Cancer of the Colon and of the Rectum

Cancer of the large intestine comprises about 15 per cent of all cancers Of cancers of the gastro intestinal tract one half occur in the stomach 10 per cent in the esophagus 10 per cent in the colon and 25 per cent in the rectum Of cancers of the large intestine some 6 per cent are found in the cecum 17 per cent in the ascending transverse or descending colon, 13 per cent in the sigmoid 18 per cent in the

rectosigmoid and 45 per cent in the rectum Cancer of the large intestine occurs at all ages but two thirds of the patients are over age 50 and the average age reported by Rankin is 57 years It is more frequent in males than in females and less frequent in Negroes than in whites

As in the case of all cancers the ultimate cause is unknown Many but by no means all cancers of the colon develop from adenomatous polyps These polyps are often multiple and so may give rise to multiple or recurrent cancers In the cecum and ascending colon the tumor is usually a soft fungating ulcerating medullary carcinoma that does not cause obstructive symptoms The reason for this lies in the character of the growth as well as in the fact that in the proximal colon the stool is still liquid so that it readily passes through a partially narrowed lumen In the distal colon one encounters most often an annular fibrous growth that greatly narrows the lumen Obstructive symptoms follow because the feces which in this portion of the colon are solid cannot pass the stricture In the rectum an adenocarcinoma is the usual lesion Metastases spread first to the regional lymph nodes and then to the liver

The symptoms depend on the location and the character of the lesion Tumors of the cecum and ascending colon do not obstruct the lumen of the bowel and therefore do not cause colic and severe cramps Very often they give rise to no local disturbances Secondary anemia and weakness may be the only manifestations for many months Some patients complain of vague indigestion and abdominal distention At times there is pain in the right lower quadrant of the abdomen and very commonly the mistaken diagnosis of chronic appendicitis is made until operation reveals the true state of affairs

Rankin F W and Graham A S *Cancer of the Colon and Rectum* (Springfield Ill Charles C Thomas Publisher 1939)

A mass becomes palpable in about one half of the cases

When the new growth involves the left half of the colon, symptoms of motor disturbance of the large bowel characterize the clinical picture Colicky abdominal pain occurs when there is partial obstruction of the lumen of the colon Constipation develops and there is intermittent diarrhea The sudden onset of constipation or of constipation alternating with diarrhea should always arouse suspicion of cancer of the large intestine Bleeding is frequent and then bright red blood appears in the stool Abdominal palpation may reveal a mass but usually this is absent Rectal examination is negative unless there are metastases in the rectal pouch or pelvis

Commonly the lesion grows slowly and months may elapse before the symptoms are sufficiently distressing to impel the patient to visit the physician or to arouse the suspicion of the physician who has been treating such a patient Indeed most patients with cancer of the colon have had symptoms for about a year before operation is finally undertaken A valuable sign pointing to carcinomatous ulceration of the bowel is the discovery of occult blood in the stool by the guaiac test which can be performed in any physician's office Such a finding is significant even if the patient has been eating meat

A small particle of feces is stirred in a few centimeters of water and 15 drops of glacial acetic acid added A fresh solution of gum of guaiac is made in alcohol and 15 drops of this tincture and 5 drops of hydrogen peroxide are then added to the stool mixture Development of a blue color indicates the presence of blood Repeated positive guaiac tests indicate bleeding into the gastro intestinal tract and if some local cause such as hemorrhoids can be excluded point to an ulcerating lesion usually a neoplasm

Roentgen study with a barium enema the only accurate diagnostic procedure should be carried out whenever there

is the slightest suspicion of a colonic lesion It is unwise to *give barium by mouth for the barium mass may induce intes*tinal obstruction Negative roentgen findings do not exclude the presence of carcinoma of the colon and if the clinical symptoms point to colonic neoplasm roentgen examination should be repeated at short intervals At times an exploratory operation may reveal a lesion undisclosed by the roentgen examination For a full year I observed one patient who persistently had occult blood in the stool and whose only symptom was secondary anemia that temporarily responded to iron therapy Three barium enemas gave negative results but the fourth at the end of 12 months after he had had a severe intestinal hemorrhage revealed a cancer of the cecum He was operated on and remained well for three years then died of coronary occlusion

Complete intestinal obstruction and acute perforation of the colon as a result of carcinoma are rare Chronic perforation with localized abscess formation is more common

Cancer of the rectum or rectosigmoid juncture gives rise to disturbances similar to those induced by lesions of the left side of the colon A sudden change of bowel habit is the most significant symptom If the lumen of the bowel is obstructed there are colicky cramps Constant boring pain results from invasion of the surrounding structures Hemorrhage with bright red blood in the stool occurs in almost every case Doctor and patient too readily attribute such bleeding to hemorrhoids which are so often present There is absolutely no excuse for this mistake which results only from inattention or carelessness on the part of the physician Cancer of the rectum is readily diagnosed by rectal examination and many cases would be recognized at an early operable stage *if a rectal examination were carried out on every patient with* disturbances of the bowels In addition a sigmoidoscopic



Fig 80 —Intestinal obstruction due to carcinoma of the *sigmoid* Note the colon distended with gas

examination should be performed and a specimen of a suspicious lesion removed for pathological examination

The prognosis for cancer of the colon and rectum depends largely on the feasibility of surgical removal As in all cancers early diagnosis is the most important element The size of the lesion has little influence on the outcome but some neoplasms are by nature more malignant than others The prognosis is best for cancer of the cecum and grows progressively worse the lower the lesion is in the large bowel being worst in the case of cancer of the rectum Much depends on the skill and knowledge of the surgeon Surgeons who have had much experience with these new growths find that about 70 per cent of them are operable and that the operative mortality is about 10 per cent They report five year cures in one half of the operated cases In the case of cancer of the rectum the figures are a little less favorable

Treatment —In the absence of manifest metastases operation should be done even in late cases for neoplasms of the large bowel are slow growing and metastasize late and cures are not infrequent Advanced age is no contraindication to operation Most important is careful preoperative preparation Attempts are made to empty the partially obstructed bowel at first with mild laxatives such as milk of magnesia or mild saline cathartics and colon irrigations Meanwhile the patient is given a diet low in residue Every effort is made to improve his nutrition and if there is dehydration saline and glucose infusions are given into the veins Transfusions are given to correct anemia The operation of choice is the two stage procedure with preliminary drainage and decompression of the colon proximal to the lesion When cancer of the rectum is inoperable roentgen or radium therapy may give relief by restoring a partial lumen to the bowel and controlling infection and ulceration

Hemorrhoids

Hemorrhoids are a common complaint of older persons Constipation and the enema and cathartic habit often aggravate the distress caused by them and painful hemorrhoids increase the degree of constipation Bleeding continued for many months not infrequently leads to secondary anemia Blood regeneration in the aged is not as active as in the young and they do not stand the continuous drain of blood With bleeding or with prolapse of internal hemorrhoids the simple measures of rest care of the bowels administration of mineral oil and use of demulcent suppositories should first be tried Many internal hemorrhoids can be treated successfully by injection of a sclerosing solution This is the treatment of choice in elderly individuals If this is impossible because of the size and extent of the hemorrhoids operation may have to be undertaken In every case of hemorrhoids rectal and sigmoidoscopic examinations should be done Commonly bleeding and pain attributed to hemorrhoids are due actually to a lesion higher up often a cancer of the rectum

Appendicitis

Appendicitis is chiefly a disease of youth In a recent series of 4 207 cases reported by Boyce[8] only 10 per cent occurred in persons 40 years of age or over But these cases provided 27 5 per cent of the total mortality The seriousness of appendicitis increases with age The case mortality of appendicitis in the fifth decade is 12 per cent in the sixth decade 15 per cent in the seventh decade 17 per cent and in the eighth decade 14 per cent Appendicitis occurs with sufficient fre

[8] Boyce F F Acute Appendicitis in Middle and Late Life Am J Digest Dis 8 223 June 1941

quency in older life to be a potential danger and to demand constant alertness on the part of the physician when he sees patients with abdominal complaints

In older patients early and massive gangrene of the appendix which may extend to the cecum and a spreading peritoneal infection are common This is supposedly due to greater involvement of the appendical blood vessels The *symptoms of appendicitis in old people may be minimal and* they rarely follow the textbook description Often the onset is marked by diarrhea and periumbilical pain There may be nausea but vomiting is commonly absent The pain may not be localized to the right lower quadrant but local tenderness on pressure in the right lower quadrant or by rectal palpation is often elicited The abdomen is apt to be soft and distended and rigidity may be lacking In over half the cases the temperature does not rise above 100 F and the pulse rate may not go above 90 The symptoms may suggest incomplete intestinal obstruction The white blood cell count may not reveal much leukocytosis If the condition is unrecognized in its early stages a large appendical abscess may form and the patient may present himself with an abdominal mass and obstructive symptoms that may suggest a neoplasm All older patients with abdominal pain or distress should be kept under close observation and the use of cathartics must be absolutely interdicted Early consultation with a surgeon should be had and every case should be evaluated with utmost care Once the diagnosis of acute appendicitis is reasonably certain immediate operation is indicated

Diaphragmatic (Hiatus) Hernia

Diaphragmatic hernia also known as hiatus or paraesophageal hernia occurs in two forms Ten per cent of cases

are due to a congenitally short esophagus that draws all or part of the stomach into the thorax Such anomalies of course are found in infants although they may not be discovered until late in life The common form of diaphragmatic hernia is due to an enlargement of the diaphragmatic hiatus through which the esophagus passes which allows part of the cardia of the stomach to herniate into the thorax Some few cases are due to trauma but in most instances atrophy and relaxation of the hiatus musculature together with elevated abdominal pressure favor the development Passage of the stomach into the thorax is favored by the horizontal position The longitudinal muscle fibers of the lower esophagus are continuous with the longitudinal fibers of the stomach Experimentally electric stimulation of the vagus as well as vagus reflexes induced by irritation of various abdominal viscera causes contraction of these muscles sufficient to pull the stomach up through the hiatal orifice In humans the symptoms of hiatus hernia are intermittent and the herniation as demonstrated by the roentgen examination may appear and disappear It has been suggested[8] that recurrences of hiatal herniation may result from vagus stimulation arising reflexly from a diseased abdominal viscus e g gall bladder disease or psychogenically in persons with autonomic imbalance Diverticula of the esophagus stomach or small or large intestine are common in patients with diaphragmatic hernia There may be interference with the blood supply of the herniated sac giving rise to congestion of the mucous membrane with bleeding erosions and even ulcers or major hemorrhage The average age of patients in whom diaphragmatic hernia is discovered is 60 years and fully 60

[8] Gilbert N C *et al* Recurrent Hiatus Hernia" J A M A 132 131 Sept 21 1946

per cent of them are over 50 years of age Eighty five per cent of cases occur in women

There may be no symptoms Commonly the patient complains of high epigastric or low substernal distress on eating particularly after a heavy meal Lifting or straining by temporarily increasing the herniation may induce similar symptoms This discomfort is particularly apt to come with recumbency and the patient often suffers at night and finds relief when he gets up and walks about Regurgitation of food is common and with it the distressing symptoms are relieved At times the pain may be high under the sternum and may radiate to the left shoulder and even down the left arm thus simulating the anginal syndrome The differential diagnosis between the two conditions may be difficult When anginal pain occurs immediately after meals and during meals if the patient finds relief by moving about and if there is regurgitation of food the possibility of a diaphragmatic hernia should always be considered

Secondary anemia is common due usually to slow continuous loss of blood from the congested mucous membrane of the hernial pouch At times severe hemorrhage may take place and a peptic ulcer may occur in the herniated portion of the stomach

Diagnosis rests exclusively on roentgen examination and special technics must be employed to visualize the lesion Fluoroscopic examination without the opaque meal should be done first because in some instances ingestion of food may bring about reduction of the hernia Search should be made for a gas containing shadow just above the level of the diaphragm After ingestion of the barium meal the patient should be examined in the recumbent or Trendelenburg position

Treatment with small frequent feedings of a soft bland diet often brings relief from symptoms The patient should

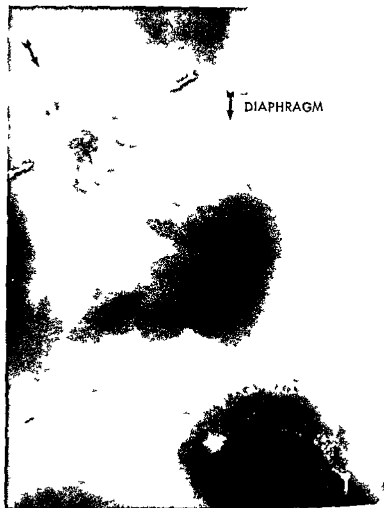


Fig 31 —Diaphragmatic (hiatus) hernia

not lie down after meals and should sleep with the head and thorax elevated Activities that increase intra abdominal pressure such as lifting stooping or straining at stool should be avoided When these simple measures bring no relief section of the phrenic nerve to induce paralysis of the diaphragm may abolish the symptoms If this too is unsuccessful recourse may be had to surgical closure of the esophageal hiatus

Hernia

Although hernias occur from infancy onward they become more frequent with advancing age and become an increasing cause of disability and death Landers[9] in an examination of over 3 500 workmen found a total incidence of hernia of 10 per cent Among men under age 50 the frequency was 8 per cent among those over 50 it was 29 per cent Twenty three per cent of men in the decade 51 to 60 and 41 per cent of those between 61 and 70 had hernias In one quarter of all cases there were bilateral hernias and one quarter of the men had been operated on and had recurrences In view of this age distribution it seems unlikely that hernia in older persons can be ascribed to congenital weakness of the structures Certainly weakness and atrophy of the supporting musculature and fascia must play an important role Hernia commonly develops in persons with chronic bronchitis and emphysema The incessant cough strains the weakened structures of the abdominal wall until they give way Inguinal hernia is much more common in men than in women but umbilical hernia occurs more frequently in women particularly in those who are obese and who have pendulous abdominal walls Femoral hernia occurs most

[9] Landers M B Jr Age Incidence of Hernia Indust. Med 7 671 November 1938

commonly after the age of 60 Postoperative ventral hernias are also more common among elderly persons

Aside from the fact that hernias gradually become an intolerable nuisance to the patient they are a constant source of danger because of the frequency with which incarceration or strangulation occurs These complications develop more often in the aged and carry with them a high mortality In elderly persons too are encountered large scrotal and umbilical hernias which by their weight and mass cause much discomfort to the patient

Treatment —The treatment of hernias in older persons is not very successful Dulin[10] reporting on 300 herniorraphies in patients over age 60 found an operative mortality of 3 8 per cent in elective operations This is seven times the mortality of patients under 60 in the same hospital There was recurrence of the hernia in over 20 per cent of cases three times as frequently as among the younger age groups Grace and Johnson[11] report a similar experience The reasons for the higher operative mortality lie in the associated diseases that are so commonly found in older persons chiefly coronary artery disease prostatic enlargement and pulmonary emphysema Postoperative pulmonary embolism is much more frequent in older patients The increased tendency to recurrence is attributable to the weakened musculature and lessened power of repair of the aging body

These figures indicate that the time to cure hernias by operation is when the patient is young before he has passed his fiftieth year Vigorous prosecution of this policy will prevent much disability and save many lives later The treatment

[10] Dulin J W "Inguinal Hernioplasty in the Aged" J Iowa M Soc 28 239 June 1938

[11] Grace R V and Johnson V S "Results of Herniotomy in Patients More Than Fifty Years of Age" Ann Surg 106 347 September 1937

of hernias in elderly persons should be highly individualized In a patient in his sixth decade who is well preserved for his years operation is the method of choice But if there are associated disorders of the cardiovascular system or of the lungs or if the patient is past the age of 60 operation is best avoided Every attempt should be made to control the hernia with a truss or appropriate belt In the case of the femoral hernias however because of the anatomical nature of the herniation a truss is unsuitable If incarceration occurs the physician should attempt gentle reduction If this succeeds the problem arises whether or not operation should be carried out to prevent a recurrence of the complication or even a possible strangulation Much depends on how successfully the hernia can be retained by a suitable truss Strangulated hernia calls for emergency operation As with all cases of intestinal obstruction *hours count in these cases* and every delay greatly increases the mortality In herniorraphies as in all operations on elderly persons the physician must remember the great frequency of phlebitis and pulmonary embolism After the operation the patient should be made to move his legs frequently from the very first and the nurse should carry out massage and passive movements of the legs

Often the patient insists on operation because the rupture makes his life miserable or impedes him in his work The risks of the operation and the frequency of recurrence should be explained to him before he is hurried to the surgeon Often a readjustment of his truss will give him relief If he has a chronic cough operation is most inadvisable for a recurrence of the hernia is almost certain

Chapter Twelve

DISEASES OF THE BILE PASSAGES, LIVER AND PANCREAS

GALLSTONES

GALLSTONES are found at autopsy in approximately 10 per cent of all persons over the age of 20 Their frequency increases with each decade of life reaching an incidence of 29 per cent in women between the ages of 61 and 70 In men of this same decade the incidence is 11 per cent In the younger age groups gallstones occur seven times as frequently in women as in men With advancing years there is a relative increase of cholelithiasis in men so that the ratio drops to about 3 1 Gallstones are less common in Negroes than in whites particularly in males Gallstones may be completely silent throughout the life of the patient Estimates as to the frequency with which they cause symptoms vary from 10 to 100 per cent of all carriers of gallstones

Often they do not provoke the classic symptoms of gallstone colic but give rise to rather nondescript complaints of indigestion The patient suffers from flatulence belching nausea and distention Eating is soon followed by bloating and epigastric oppression and often by heart burn The symptoms may simulate those of peptic ulcer but they lack the

classic periodicity in relation to eating that is observed in patients with peptic ulcer Many patients complain of dull pain in the right hypochondrium and some of rheumatoid pains in the right shoulder and arm Commonly there is in tolerance of certain foods Each patient has his own idiosyn crasies The gastric acidity is usually low and constipation is the rule

Gallstone colic is more easily recognized The patient expe riences sudden severe sharp cramplike pain in the right hypochondrium or in the epigastrium which radiates to the right and to the back the scapular region and the right shoulder It may spread across the abdomen to the left The pain is so intense that the patient doubles up and often breaks out in a sweat Vomiting is common The pain lasts from three to 12 hours and its intensity may wax and wane Fi nally it subsides leaving some residual soreness for a day or two Recurrences are the rule They may be frequent every few days or weeks or they may come at intervals of months or years Commonly there is a series of attacks followed by a long free interval Jolting of the patient such as experi enced in an automobile ride over rough roads or indiscretion in eating may induce attacks

Acute cholecystitis may follow the gallstone colic In such cases fever and leukocytosis develop and tenderness and rigidity become manifest in the right upper quadrant of the abdomen The acute inflammation of the gallbladder sub sides gradually within a week or two Gangrene of the gall bladder occurs in about 0 7 per cent of cases of cholecystitis Rarely rupture of the inflamed viscus takes place giving rise to peritonitis which is usually fatal In other instances some fever and tenderness persist the gallbladder gradually becomes distended with pus and the so called empyema of the gallbladder becomes palpable

Acute cholecystitis and its sequelae may occur in the absence of gallstones In contrast to the usual form of cholecystitis this is more common in males There is no previous history of the digestive disturbances that accompany gallbladder disease The acute cholecystitis is often preceded by an upper respiratory or another infection and it is believed that the gallbladder may be infected through hematogenous channels This form of cholecystitis is commonly quite severe

Gallstones are found in the common bile duct in from 10 to 20 per cent of cases of cholelithiasis that come to operation In two thirds of the cases there is only one common duct stone in the rest there are multiple stones Most of these stones have passed from the gallbladder through the cystic duct They may be quite small when they enter the common duct and then grow by accretion More rarely stones may form in the common bile duct Intrahepatic stones are quite unusual The stones may cause complete or partial obstruction of the common duct with resulting jaundice The extrahepatic bile ducts become dilated while the gallbladder is small and shrunken Commonly infection of the bile ducts sets in The cholangitis may be acute and fulminating or may run a more insidious course Such cholangitis persisting for years leads eventually to biliary cirrhosis—a clinical picture with irregular fever jaundice an enlarged hard liver and a large spleen If a stone becomes impacted in the ampulla of Vater bile may regurgitate into the pancreatic duct and lead to acute hemorrhagic pancreatitis More commonly chronic interstitial pancreatitis is found in long standing cases

When the stone enters the common duct jaundice usually develops This complication is so frequent and may be so serious that the physician should always be on the lookout for jaundice in patients with gallstones particularly immedi

ately after an attack of colic Obstruction of the duct may be complete and result in acholic stools but more often obstruction is partial If the stone is freely movable in the common duct it may have a ball valve action giving rise to intermittent attacks of pain and jaundice with the icterus clearing and the stools becoming colored again in the intervals With lodgment of the stone in the common duct the attacks of pain may cease and jaundice may be the only symptom In fully one quarter of cases in which stones are found in the common duct there has been no jaundice A gallstone may enter and obstruct the common bile duct without the patient ever having had attacks of colic but usually with stones in the common duct attacks of colic persist In rare cases the stone may be discharged into the duodenum with subsidence of symptoms Chills and fever usually appear when a stone enters the common bile duct

Diagnosis —Diagnosis of cholelithiasis or chronic cholecystitis depends in the first place on painstaking evaluation of the symptoms Physical signs are usually inconclusive in the absence of jaundice or acute inflammation of the gall bladder A definitive diagnosis cannot be made without roentgen examination Cholecystography should be done whenever there is reason to suspect gallbladder involvement except in the presence of jaundice The demonstration of stones on the roentgen films is conclusive Lack of visualization of the gallbladder practically always indicates gall bladder disease if the technic has been adequate A double dose of the dye should always be given and accurate technic is essential Poor films lead to errors in diagnosis Poor visualization of the gallbladder as represented by a light shadow or delayed emptying has little significance and no diagnosis should be based on such findings The discovery of gallstones by means of the roentgen examination does

not prove that the patient s symptoms are caused by the stones Often such stones may be silent and the patient may be suffering from an altogether different ailment The roentgen findings should be closely correlated with the symptomatology and the physical findings Often it will be necessary to make parallel roentgen studies of the gastro intestinal and urinary tracts before a diagnosis can be reached

An older person who is already jaundiced when first seen presents a difficult problem in diagnosis The common lesions that cause jaundice in the later years of life are gallstones in the common bile duct carcinoma of the head of the pancreas carcinoma of the liver and acute hepatitis It is essential to distinguish between these several conditions operation may save the life of the patient with common duct stone but may cause death in a patient with hepatitis

The symptomatology gives a valuable clue to the diagnosis Gallstones usually but not always make themselves known by attacks of pain carcinoma of the pancreas and hepatitis are usually painless but hepatitis may commence acutely with severe abdominal pain and vomiting A history of severe alcoholism or of treatment with cinchophen or one of its derivatives or with one of the arsphenamines suggests the possibility of hepatitis

Hepatitis is relatively uncommon in older patients but should be kept in mind Hepatitis causes incomplete obstruction of the bile ducts If the stools are examined daily some bile will be found from time to time although the stools may be completely acholic for a few days Carcinoma of the pancreas causes complete obstruction with jaundice progressively increasing until the skin has a deep greenish hue The stools are completely acholic A stone in the common duct causes complete jaundice only if it is impacted in the ampulla of Vater Usually complete obstruction is

transient and bile is found in the stools from time to time if they are repeatedly examined

With complete obstruction of the common duct there is no urobilin in the urine with incomplete obstruction as in hepatitis urobilin is always found in the urine With obstructive jaundice the blood cholesterol and cholesterol esters are increased with hepatitis they are both decreased particularly the esters The results of liver function tests such as the galactose tolerance and the cephalin flocculation tests are normal in obstructive jaundice unless the condition is of long duration with secondary liver damage in the case of hepatitis they are abnormal

As a rule careful evaluation of the symptomatology and of these tests will yield the correct diagnosis But at times in spite of painstaking study an incorrect diagnosis is reached I recall a man aged 58 in whom all signs pointed to obstructive jaundice due to stone Operation was scheduled but on the same day the patient experienced a cerebral hemorrhage so it had to be postponed While the patient was recovering from the cerebrovascular insult his jaundice cleared and never returned Manifestly he had had hepatitis Conversely one sees patients with persistent jaundice apparently caused by carcinoma of the head of the pancreas who are cured by operative removal of a common duct stone Whenever the diagnosis is in doubt an exploratory operation should be undertaken for the clinical diagnosis is too open to error

Fifty years ago when operation was not lightly undertaken and the clinician saw many more patients with jaundice of long duration due to gallstones Naunyn established the following criteria for the diagnosis of common duct stone as the cause of jaundice the continuous or intermittent presence of bile in the stool variation in the intensity of the

jaundice little or no hepatic enlargement, absence of a palpable gallbladder enlargement of the spleen without ascites, fever duration of the jaundice for more than a year These criteria are still as sound as they were fifty years ago

With stones in the common duct infectious cholangitis may develop The patient becomes very ill with chills and high intermittent fever and jaundice increases

Fistulas may form between the gallbladder and the surrounding structures in long standing neglected cases of cholelithiasis The gallbladder may become adherent to the anterior abdominal wall and an abscess of the abdominal wall may develop which may eventually spontaneously discharge so that gallstones are extruded through the skin More commonly, the diseased gallbladder becomes adherent to the duodenum or colon and cholecystoduodenal or cholecystocolonic fistulas form In this manner very large gallstones may be discharged from the gallbladder into the gastro intestinal tract If they enter the colon they are ordinarily passed in the stool If they enter the duodenum and this is the most frequent site of internal biliary fistulas they may cause intestinal obstruction From 1 to 5 per cent of all cases of intestinal obstruction are caused by gallstones, most frequently in women past the age of 60 Roentgen examination discloses the diagnosis in most cases [1] It reveals the dilated loops of small intestine characteristic of complete or partial intestinal obstruction and the presence of air in the gallbladder and bile ducts At times the stone may be visualized or a change in position of a stone previously observed may be noted Gallstones should always be thought of as a possible cause of ileus in older women Prompt recognition and operation will save life

[1] Rigler L. G Borman C N and Noble J F "Gall Stone Obstruction" J A M A 117 1753 Nov 22 1941

Diseases of the gallbladder and of the heart are so often associated that many authors assume a causal relationship between the two conditions Statistical evaluation of this relationship disproves this assumption Both disorders are so common in the later periods of life that concurrent disease in the two organs is often encountered In certain syndromes there is a relationship between disorders of the gallbladder and of the heart Extrasystoles and paroxysmal auricular fibrillation or tachycardia may be induced reflexly by a diseased gallbladder and such symptoms may subside after cholecystectomy Pain arising in a diseased gallbladder may simulate the pain of angina pectoris and it may be difficult to determine which of the two organs is giving rise to the symptoms It has been shown experimentally in human subjects that inflation of the common bile duct by means of a rubber balloon may cause pain referred to the precordium In the presence of a normal heart it is unusual for the pain of gallbladder disease to radiate to the precordium In patients who have both gallbladder disease and coronary artery sclerosis the pain provoked by the cholecystic disease may radiate to the precordium and left arm the pain from the gallbladder radiates down the sensitized cardiac pathways At times gallbladder disease may give rise to anginoid pains and T wave changes in the electrocardiogram and after cholecystectomy the precordial pain may completely disappear and the electrocardiogram return to normal

Treatment —Silent gallstones that are discovered accidentally and give rise to no symptoms should be ignored but the patient should be told of their presence in case obscure symptoms arise subsequently In patients with indigestion gas and mild irregular pains medical treatment should be instituted A bland diet poor in fat is best tolerated If the patient is obese the diet should be planned to insure reduction in

weight Bile salts often are valuable in relieving pain and dyspepsia and in correcting constipation They should be given in 5 gr capsules with meals Good preparations are bilron and procholon The dosage varies from 5 to 20 gr three times a day Enough should be given to relieve constipation In the presence of jaundice bile salts may increase itching of the skin When constipation persists a mild saline cathartic such as sodium phosphate every morning is useful Atropine gr 1/150 or tincture of belladonna 15 drops three times a day often relieves pain due to spasm Trasentin and syntropan have the antispasmodic effect of atropine with fewer side effects Their action may be reinforced with phenobarbital

Gallstone colic gives rise to intense pain It may be promptly relieved by nitroglycerin gr 1/100 under the tongue or by inhalation of amyl nitrite The dose may be repeated within a few minutes If nitrites give no relief recourse must be had to full doses of morphine After the attack the treatment outlined for cases of gallstones with milder symptoms should be carried out

Indications for operation are difficult to draw precisely Experience has shown that in the absence of calculi cholecystectomy commonly brings about no relief of symptoms Similar poor results are obtained when gallbladders are removed that the roentgenologist reports as showing only faint visualization or delayed emptying Simple motor disturbances of the gallbladder and sphincter of Oddi may give rise to symptoms of gallbladder disease and these are not relieved by operation It is a good rule not to operate if the roentgen picture shows a well filled gallbladder without stones But the roentgen study is not infallible Gallstones that did not show on the roentgen film may be found at operation and inflamed gallbladders have been encountered at operation

that gave a normal roentgen picture At times the physician is compelled to rely on his unaided clinical judgment When gallstones are demonstrated on the roentgen film or when the gallbladder is not visualized and when a period of conscientious medical treatment has brought the patient no relief operation should be undertaken and cholecystectomy is the procedure of choice It is unwise to hurry an older patient to the operating table just because he has had an attack of gallstone colic But if attacks frequently recur operation is called for Jaundice should be sought for after every attack of biliary colic With the occurrence of jaundice pointing to stone in the common duct operation becomes imperative unless the icterus subsides within a few days Even when it disappears within a short time the stone has probably remained in the common duct and a return of the icterus may be expected and operation usually becomes necessary When infection accompanies biliary obstruction operation is urgently indicated At operation the common duct should always be exposed and explored by palpation else many common duct stones will be missed In the presence of jaundice or when the common duct is dilated or inflamed or the head of the pancreas is hard the common duct should be opened and explored for stones

Cholecystitis should be treated conservatively especially in older patients With bed rest fluid diet and application of an ice bag to the abdomen the inflammation subsides in one or two weeks Immediate operation should be carried out only if there are evidences of progressive infection or of development of empyema of the gallbladder It is safe to wait a few days to see whether or not there is spontaneous subsidence of the inflammation Persistent fever leukocytosis and unrelieved pain tenderness and rigidity over the gallbladder region give evidence that the infection is not re

solving When operation becomes necessary in the acute stage cholecystostomy is often the procedure of choice After the subsidence of an acute cholecystitis it is usually wise to remove the gallbladder

In all cases of biliary disease appropriate preparation for operation is of the greatest importance All patients with hepatic disease should be given a diet rich in carbohydrates 300 to 600 Gm a day This has a glycogen sparing action on the liver If the patient cannot take enough carbohydrate by mouth glucose in 5 or 10 per cent solution should be given intravenously Intravenous administration of glucose should be part of the routine preparation for operation in these cases and should be continued for several days post operatively Commonly the prothrombin content of the blood is reduced leading to a hemorrhagic tendency This should *be corrected by the administration of vitamin K* It is given in dosage of 1 to 2 mg three times a day Good preparations are proklot and clotogen To insure maximum absorption of vitamin K it is best to give bile salts simultaneously Within two or three days the prothrombin level returns to normal This should be controlled by determining the prothrombin time

Cancer of the Gallbladder

Cancer of the gallbladder is found in about 0 9 per cent of gallbladders removed at operation[2] Gallstones are the chief predisposing cause of this growth and 90 per cent of all cancers of the gallbladder are found in gallbladders containing stones Accordingly the condition is more common in women The growth is an adenocarcinoma in 85 per cent

[2] Vadheim J L Gray H K and Dockerty M B "Carcinoma of the Gall Bladder" Am J Surg 63 151 1944

of cases a squamous cell carcinoma in 3 per cent The average age of patients with cancer of the gallbladder is 58 years The symptoms are not characteristic and preoperative diagnosis is rare Typically the patient is a woman with a history of repeated gallstone colic or of the digestive disturbances associated with gallbladder disease who for some months has complained of continuous pain in the right upper quadrant of the abdomen, with anorexia and loss in weight In other cases there are few local symptoms and distant metastases may overshadow the clinical picture A mass in the region of the gallbladder is found in about half of the cases Jaundice is common and is usually caused by pressure of tumor masses on the common bile duct more rarely by extensive liver metastases Secondary anemia is uncommon in these cases

Diagnosis rests on the history and the discovery of a mass in the right upper quadrant of the abdomen The gallbladder is not visualized when roentgen films are taken after the administration of dye In the early operable stages diagnosis can be made only on the operating table The physician can ascertain only that there is disease of the gallbladder Carcinoma of the gallbladder is highly malignant and most patients die within one year after operation The only hopeful cases are those in which the pathologist unexpectedly discovers an early lesion in a gallbladder removed for another condition As a rule the growth spreads to the regional lymph nodes and to the liver and jaundice and ascites follow The neoplasm may ulcerate into the colon At this stage no treatment is helpful

Primary carcinomas of the hepatic ducts or of the ampulla of Vater give rise to symptoms of partial or complete obstruction of the common duct They are rare conditions

The symptoms of carcinoma of the ampulla of Vater often arise acutely with biliary colic and jaundice The tumor usually grows into the duodenum where it may ulcerate Portions of the tumor may slough off and give transient relief to the common duct obstruction and to the jaundice Often intestinal hemorrhage accompanies this ulceration There is commonly an accompanying cholangitis The gall bladder becomes distended and may be palpable Roentgen study may reveal abnormalities of the second portion of the duodenum which together with the intermittent jaundice and intestinal bleeding may suggest the diagnosis of carcinoma of the ampulla of Vater Palliative operation consists in cholecystogastrostomy to relieve the common duct obstruction Complete removal of the neoplasm is accomplished by Whipple s procedure At a first stage operation a posterior gastro enterostomy and ligation of the common bile duct with cholecystogastrostomy are carried out At a later date the duodenum the head of the pancreas and the common duct are excised in one mass Some recoveries have been reported

Degenerative Liver Diseases

Cirrhosis of the liver occurs at all ages About one half of the patients are over the age of 50 at the onset of their symptoms If a correction is made for the age composition of the population cirrhosis of the liver has its highest incidence between the ages of 55 and 59 [3] Its symptomatology resembles that of the disease in younger persons Hepatitis and acute yellow atrophy are unusual in the older age groups

[3] Ratnoff O D and Patek A J Jr "The Natural History of Laennec s Cirrhosis of Liver" Medicine 21 207 September 1942

Carcinoma of the Pancreas

Cancer of the pancreas occurs chiefly after the age of 50 and over twice as frequently in men as in women In fully 80 per cent of the cases it is situated in the head of the pancreas Except for the fact that jaundice develops when the growth obstructs the common bile duct the symptoms are much the same no matter what the site of the tumor Pain is usually the earliest as well as the chief symptom It is in the epigastrium the left upper quadrant or the back in the left lumbar region The pain is constant and may be severe It is worse when the patient is lying down and accordingly commonly disturbs him at night and awakens him from sleep Sitting up or leaning forward or *lying on the side with the* legs drawn up often relieves the pain Jaundice develops sooner or later in about three quarters of the cases The biliary obstruction becomes complete the stools are acholic and there is no urobilin in the stool The jaundice gradually deepens until the skin acquires a deep greenish yellow hue In half the cases a distended gallbladder is palpable (Courvoisier s law) Rapid and great loss of weight is almost constant Anorexia nausea and vomiting are common Diarrhea may occur An abdominal mass is palpable in about one third of the cases and ascites occurs in 10 per cent Anemia is usually absent or slight and there is no occult blood in the stool The sedimentation rate of the red blood cells is rapid Glycosuria may be present Some patients exhibit anxiety insomnia and depression to such an extent that in the absence of physical signs the incorrect diagnosis of psychoneurosis may be made

Diagnosis—Rapid unexplained loss of weight associated with persistent pain in the upper portion of the abdomen or left lumbar region should arouse suspicion of carcinoma

of the pancreas[4] When with this jaundice develops and the gallbladder becomes palpable the diagnosis becomes almost certain At times there may be only the clinical picture of painless jaundice Roentgen study is often helpful First it excludes organic disease of the gastro intestinal tract The roentgen film may reveal obstruction or irregularity of some part of the duodenum or a spreading of the semicircular course of the duodenum as it embraces the head of the pancreas A certain diagnosis can be made only at operation or at autopsy

Treatment—Surgical cure should be attempted The Whipple operation of resection of the pancreas and duodenum after preliminary gastro enterostomy and cholecystogastrostomy offers some hope in the future Chronic pancreatitis may simulate cancer of the head of the pancreas and it may be impossible to distinguish between the two even at the operating table Simple cholecystogastrostomy will relieve jaundice and prolong the life of the patient with cancer of the head of the pancreas it may cure the patient with chronic pancreatitis But the prognosis for cancer of the pancreas is still very poor The average duration of life from the onset of symptoms to death is about seven months

Acute Pancreatitis

Over half the cases of acute pancreatitis occur in persons over the age of 45 the average age in a recently published series was 57 8[5] It occurs a little oftener in women than in men and is often associated with cholelithiasis but rarely with diabetes The cause in most instances is unknown only

[4] Berk J E "Diagnosis of Carcinoma of the Pancreas" Arch Int Med 68 525 September 1941

[5] Johnson W M and Davis O T Pancreatitis in Geriatric Practice Geriatrics 1 125 Mar Apr 1946

rarely is the mechanism described by Opie operative—blockage of the ampulla of Vater by a gallstone with regurgitation of the bile into the pancreatic duct Vascular occlusion is said to be responsible in some cases

The onset is sudden with intense epigastric pain that may radiate to the back or to the left and with severe vomiting There are marked tenderness and some rigidity in the epigastrium but never the boardlike rigidity associated with perforated ulcer Fever is not present initially but appears in a few days as does leukocytosis The hyperacute stage usually lasts one or more days and the symptoms gradually subside but may persist for several months A palpable mass may develop in the epigastrium and may be visualized on roentgen examination by the spreading of the C shaped loop of the duodenum

Diagnosis on clinical grounds alone is difficult for the symptoms may suggest cholecystitis ruptured peptic ulcer intestinal obstruction or even coronary thrombosis Some attacks are mild and very brief The blood amylase content is always elevated in the earliest stages of acute pancreatitis but may drop to normal within 12–24 hours Determination of the blood amylase content is indispensable to diagnosis and should be carried out promptly in all suspected cases A figure of over 200 Sosmogyi units (the upper limit of normal is 150 units) is diagnostic Figures as high as 550 have been reported The elevated values are due to blockage of the pancreatic ducts and absorption of the pancreatic enzymes by the lymph and blood

Treatment is symptomatic Surgical intervention is rarely indicated except in very late stages when a pancreatic cyst may have formed Bed rest the liberal use of opiates and the administration of glucose and saline solutions intravenously if vomiting is severe is all that is needed

Chapter Thirteen

DISEASES OF THE GENITO-URINARY TRACT

Benign Enlargement of the Prostate Gland

BENIGN enlargement of the prostate is found at autopsy in one third of men between the ages of 50 and 59, in two thirds of those in the seventh and eighth decades and in three quarters of all men over the age of 80 However in only one fifth of these cases does the enlarged gland give rise to symptoms The average age at which symptoms arising from prostatic enlargement compel the patient to seek medical assistance is about 63 years The cause of this disorder is unknown but the evidence suggests that some alteration in the balance of the endocrine glands is responsible Loss of the testis and of its internal secretion as in eunuchs leads to atrophy of the prostate In men over the age of 50 there is a progressive diminution in the amount of male sex hormone and apparently an increase in female estrogenic hormone This leads to atrophy of the prostate gland Prostatic enlargement in older men is due to a nodular hyperplasia beginning in the stroma and in the periurethral glands of the middle lobe stimulated apparently by the altered balance of the sex hormones It usually arises in the middle lobe of the prostate between the floor of the urethra the bladder neck and the entrance of the ejaculatory ducts The periurethral

glands or tubules multiply and there is accompanying fibro myomatous hypertrophy The growth is an adenomyofibroma with varying amount of glandular tissue It gradually com presses and pushes aside the atrophic prostate gland which finally persists as a shell or false capsule around the growth Because of its location enlargement of the middle lobe quickly leads to urinary disturbances The growth may in volve the whole gland prostates weighing as much as 500 Gm have been removed

Symptoms —These come on insidiously The patient has to void with increasing frequency and must get up at night to empty his bladder The stream becomes halting and slow in starting and has little force Gradually in the course of years the symptoms become worse The bladder cannot empty itself completely and there is residual urine after micturition In time the bladder becomes dilated and tra beculated and diverticuli may form

Commonly the patient is not aware of the degree of uri nary retention in the bladder the residual urine may amount to several hundred cubic centimeters but the patient voids as before with difficulty but apparently adequately In time this urinary retention causes bilateral dilatation of the pelves of the kidneys and impairment of kidney function The specific gravity of urine drops and approaches 1 010 and finally the nonprotein nitrogen content of the blood increases There may be a moderate rise in blood pressure to 160 or 180 systolic There may be occasional bleeding with gross hematuria from rupture of dilated venules in the bladder

Infection of the bladder and of the kidneys is common It occurs with especial frequency after catheterization It may lead to further rapid impairment of renal function Infection may be restricted to the bladder but commonly it ascends the ureters to give rise to pyelonephritis

Complete urinary retention may occur at any time It may follow exposure to cold or wet a drinking bout or too great delay in micturition The prostatic patient should empty his bladder at frequent intervals if by some circumstance such as attendance at a theater he is prevented from doing so he may have great difficulty in starting the urinary flow

Diagnosis—The diagnosis is suggested by the symptomatology Rectal examination usually reveals an enlarged prostate gland but gives no clue to the degree of obstruction that it is causing A middle lobe may be causing serious obstruction when rectal examination gives little evidence of enlargement of the gland The residual urine should always be measured The patient empties his bladder and is then catheterized with meticulous aseptic precautions The amount of urine remaining in the bladder after voluntary micturition is measured A persistent residual urine over 50 cc indicates retention of a degree that calls for intervention Cystoscopy should always be performed This will reveal the site and nature of the obstruction and enable the operator to determine what operative procedure is best adapted to the case The presence or absence of pus in the urine will disclose whether or not there is an accompanying infection A small amount of albumin and occasional casts have little significance in older persons It is more important to determine the state of the kidney function The specific gravity of the urine is one of the best indicators of kidney function If it is above 1 020 it may be assumed that the kidneys are secreting adequately A specific gravity between 1 015 and 1 020 points to some kidney damage and figures below 1 015 give evidence of serious impairment of renal function The blood urea nitrogen figures do not rise until the specific gravity of the urine has fallen below the critical level When elevated they indicate actual renal insufficiency The phenolsul

fonphthalein test gives little additional information of value

Treatment —When there is no residual urine conservative treatment is often effective This includes prostatic massage every day or every other day Diathermy treatments with one electrode in the rectum and the other on the hypogastrium are sometimes helpful At times urethral dilatation gives relief The use of testosterone has not been followed by striking therapeutic success It is given intramuscularly in doses of 25 to 50 mg every other day Radiotherapy is of value only to reduce accompanying inflammatory swelling of the prostate It does not cause shrinkage of the hypertrophic tissue

When there is acute retention immediate relief is called for At times the patient is enabled to void by taking a hot sitz bath Catheterization is often difficult and must be very gently carried out for it is easy to traumatize the urethra and the swollen gland If the catheter does not pass easily it is best to call on a specialist for help Even he often finds suprapubic drainage of the bladder necessary Care should be taken not to empty the bladder too quickly and completely as it may cause shock and suppression of kidney function

When there is much residual urine or when there has been acute retention operation becomes necessary This always involves a certain hazard for these patients are advanced in years and often have complicating cardiovascular or pulmonary disease Yet it is astonishing how well they stand operation if given the benefit of careful preoperative treatment and a good surgeon The most important preoperative measures are restoration of kidney function and control of urinary infection Adequate bladder drainage relieves the back pressure on the kidneys and permits considerable recovery of kidney function Often the blood nitrogen figures

return to normal evidences of toxemia disappear and there is marked improvement in the condition of the patient With the use of *sulfadiazine 15 gr four times a day* or of *strepto mycin* urinary infection is usually controlled

The old two stage suprapubic prostatectomy involves suprapubic drainage of the bladder This is usually continued for three to six weeks before the patient is in condition for enucleation of the prostate It is a tedious long drawn out procedure and the final prostatectomy carries a considerable operative risk particularly when there is cardiac impair ment Old men in poor physical health refuse to subject themselves to this procedure and their physicians hesitate to urge them to do so

The introduction of transurethral resection the constant improvement in its technic and the growing understanding of its indications and limitations have revolutionized pros tatic surgery Thompson and Habein of the Mayo Clinic re ported 1 200 such operations with a mortality of 1 6 per cent Not every case is suitable for transurethral resection and the operation requires skill and experience Preliminary drainage of the bladder and kidneys is accomplished by an indwelling catheter During this period the patient can be out of bed—a great advantage in an old person He should take a large amount of fluids Usually after a few days he is ready for operation If there are kidney insufficiency and infection preoperative treatment is prolonged Operation is carried out under low spinal anesthesia which induces little drop in blood pressure Within a few days after operation the patient can get out of bed Thus the chances of phlebitis and pul monary embolism are minimized The best urologists today find that about 80 per cent of patients with prostatic en largement lend themselves to transurethral resection

Carcinoma of the Prostate

Cancer of the prostate is rare before the age of 50 and fully 80 per cent of cases occur in the seventh and eighth decades Young reports that one fifth of men seeking relief from obstruction of the vesical neck have cancer of the prostate Autopsy studies disclose an even higher incidence which increases with age Many of these growths are latent carcinomas discovered only on histologic study of serial sections of the gland The discrepancy between the anatomic and the clinical frequency of cancer of the prostate indicates that the neoplasm grows very slowly and that years may elapse before clinical manifestations of disease occur Cancer of the prostate is commonly associated with benign enlargement but there is no causal connection between the two conditions In fact the malignant growth is derived from atrophic cells of the gland and for the most part arises in the posterior lobe which is not concerned in benign hypertrophy Cancer of the prostate may occur years after a prostatectomy has been performed It arises in the so called capsule of the gland which is left behind at operation This capsule actually represents normal prostatic tissue which has been compressed by the nodular hyperplasia of the gland Thus the association of benign hypertrophy and cancer of the prostate is accidental and ascribable to the frequency with which both conditions occur in persons of advanced age

Although carcinoma of the prostate grows slowly it is highly malignant Metastasis occurs first to the pelvic and abdominal lymph nodes to the bones of the pelvis and lumbar spine and later to the lungs and liver Over one quarter of patients have metastases when first seen

Diagnosis —Cancer of the prostate gives rise to no symptoms until it interferes with urination or until local extension

or metastasis induces pain Since most carcinomas arise in the posterior lobe far from the urethra years may elapse before the growth attains a size sufficient to induce symptoms Delay in diagnosis is also attributable to the fact that elderly men are apt to ignore symptoms of urinary disturbance until they become quite disabling and because physicians neglect to do rectal examinations of their elderly patients The earliest *diagnostic sign is the presence of a small hard nodule in the* posterior aspect of the prostate gland which can be felt by the finger in the course of a rectal examination In the later stages one feels a diffuse hard nodular enlargement of the gland which may involve the seminal vesicles and extend beyond the capsule of the gland At this stage cystoscopy with biopsy examination may prove the nature of the growth

Hematuria and loss of weight are late manifestations Commonly the first symptom is bone pain particularly in the pelvis and lumbar spine caused by metastatic growths Such bone or joint pain or sciatic pain in an older man always calls for examination of the prostate gland Determination of the serum acid phosphatase has become an important clinical test Acid phosphatase is elaborated by the acinar epithelium of the prostate gland as well as by prostatic carcinoma cells both in the primary tumor and in the metastatic deposits When metastasis of such a tumor occurs acid phosphatase is released in the blood stream and the serum acid phosphatase becomes elevated The normal figures are between 3 and 6 King Armstrong units In the presence of metastatic carcinoma of the prostate the serum acid phosphatase rises and figures as high as 180 units have been reported An elevation of the acid phosphatase in the serum is a pathognomonic sign of metastatic carcinoma having its primary source in the prostate If radical prostatectomy is contemplated for prostatic carcinoma elevation of the acid

phosphatase will indicate the presence of metastases and the futility of such an operation Serial estimations of the acid phosphatase enable the physician to follow the effects of treatment in a case of cancer of the prostate with metastases When obscure bone pain or roentgen lesions are encountered or when the location of the primary neoplasm in a patient with metastatic lesions is in doubt the discovery of high figures for serum acid phosphatase proves that the primary growth arises in the prostate gland The serum alkaline phos phatase becomes elevated when there are bone metastases no matter what the origin of the growth This then gives no information as to the primary tumor

Treatment —Treatment of cancer of the prostate is still in a state of flux and wide differences of opinion are found among the experts There are some who insist that when a small hard nodule is found in the prostate gland by rectal examination and when normal serum acid phosphatase fig ures suggest that there has been no metastasis the gland should be exposed by a perineal incision a frozen section of the nodule immediately examined and if malignant growth is found perineal prostatectomy should be carried out Colston [1] who is an ardent advocate of this policy has per formed the radical operation in 20 per cent of his recent cases with an operative mortality of 5 per cent Most genito urinary surgeons find that only 5 per cent of all cases of cancer of the prostate are suitable for radical operation Moreover the duration of life without radical intervention is often many years and the alleviation of symptoms is so successful that many surgeons insist that the radical operation is never called for A further objection is that urinary incon tinence is a frequent sequel of the radical operation In Col

[1] Colston J A C "Carcinoma of the Prostate" J A M A 122 781 July 17 1943

ston's last series of 78 operations 4 patients died in the hospital 10 died of recurrence of the growth 11 were known to have recurrence and 48 were living from six months to five years after operation Cancer of the prostate occurs at an advanced age when the expectation of life is not great It may take 10 years for a small carcinomatous nodule that has been discovered in the prostate to grow sufficiently large to cause urinary symptoms The elderly man is often a poor operative risk so as a rule conservative treatment is indicated At the Mayo Clinic radical prostatectomy is not carried out Thompson[2] reports the results of transurethral resection of the prostate in 887 patients with cancer of the prostate in whom the lesion was far advanced The operative mortality was 1 per cent and 14 per cent survived at least five years

The discovery that castration will cause immediate recession of both the primary and the metastatic lesions of prostatic carcinoma and lead to remarkable clinical improvement has reopened the whole question of therapy Androgen activates the prostatic epithelium Castration removes the androgen and eliminates this stimulation The administration of sufficient doses of estrogen in some manner neutralizes androgen and brings about a similar result The effects of castration on patients with carcinoma of the prostate even on those in the advanced stage with widespread metastasis are often miraculous Almost immediately the patient feels better his appetite improves and he begins to gain weight Within one to three days all pain is gone and a bedridden patient is usually up and about within one or two weeks With this the prostate gland becomes smaller and softer and the bone and pulmonary metastases regress and may even disappear Parallel with this there is a rapid reduction

[2] Thompson G J "Transurethral Resection of Malignant Lesions of the Prostate Gland" J A M A 120 1105 Dec 5 1942

in the concentration of the acid phosphatase in the serum The patient often experiences hot flashes after orchiectomy Good results are reported in about three quarters of the patients undergoing castration Many relapse in a few months to several years This treatment is still too recent to make possible an evaluation of its ultimate role in the therapy of cancer of the prostate

Similar results can be obtained by the administration of diethylstilbestrol the female sex hormone in a dosage of from 3 to 10 mg a day Enough must be given to achieve results Reduction in the level of serum acid phosphatase is a useful guide to dosage Administration of diethylstilbestrol may induce nausea painful hypertrophy of the breasts atrophy of the penis and testicles and impotence The dosage of the drug should be kept at the lowest level that will control the cancerous growth When a satisfactory result has been attained this may be maintained by the subcutaneous implantation of pellets of estradiol benzoate

When urinary obstruction persists in spite of castration or treatment with diethylstilbestrol transurethral resection of the prostate should be carried out This gives very satisfactory results In some cases recurrence of the growth after a variable interval of time necessitates repetition of this procedure

Before the introduction of castration and treatment with female sex hormone roentgen therapy was a useful aid in controlling metastatic lesions in bones and particularly in relieving bone pain It should be employed in cases refractory to the hormone treatment Irradiation of the primary tumor in the prostate is of doubtful value

Tumors of the Bladder

Papillomas and papillary carcinomas of the bladder manifest themselves by bleeding and by frequent urgent and

painful urination They can be diagnosed only by cystoscopy *A specimen should always be removed for pathological examination* to determine whether or not the lesion is malignant They respond well to fulguration but often recur Infiltrating carcinoma of the bladder calls for radical surgery

Renal Calculi

Renal calculi *are not commonly newly formed in elderly* persons When they are encountered they have as a rule been in existence for years without giving rise to symptoms In other cases they persist because the patient has neglected to seek or follow competent medical advice or has been improperly treated The symptoms and treatment of renal lithiasis are the same as in younger persons except so far as *impaired renal function and increased operative risk in the* aged modifies the procedures to be employed In elderly persons *with silent calculi expectant treatment is the wisest* If the stones are very large or if there is much infection and if the other kidney has adequate function nephrectomy is usually preferable to nephrotomy or other more difficult and shocking operations Bilateral staghorn calculi should not be removed surgically The operative results are poor, and the patients usually die of uremia despite operation

Tumors of the Kidney

Hypernephroma the most common malignant growth of the kidney may occur at any time from childhood *to old* age Sixty per cent of cases occur between the ages of 40 and 60 It is a slow growing tumor which at first is encapsulated and by its growth causes pressure atrophy of the kidney Later it may invade the pelvis of the kidney and the

renal veins Metastases are common and have a predilection for the lungs and bones They, too may be very slow growing and may appear years after removal of the original tumor

The chief symptom is hematuria The passage of blood clots may give rise to renal colic At times bleeding may be severe enough to cause grave anemia A growth in the upper pole of the kidney escapes detection by palpation but a tumor in the lower pole can often be felt Hematuria always calls for complete genito urinary study with cystoscopy catheterization of the ureters and intravenous and retrograde urography By these means the tumor can be discovered

Because the tumor is slow growing and recurrence may be delayed many years operative removal should be attempted even when the growth seems extensive Even in the presence of a few metastases the primary tumor should be removed for this prevents further metastasis and may slow the growth of existing metastatic deposits Radiation therapy should be given postoperatively to the site of the tumor and to the metastases These patients may live for many years

The Climacteric

When they reach the age of 50 all but 12 per cent of women have entered the menopause With atrophy of the ovaries the secretion of estrogenic hormone becomes diminished and that of the gonadotrophic hormone increases The onset of the menopause is gradual and the intensity of symptoms that it may occasion varies greatly The severity of the symptoms depends a good deal upon the constitution of the patient Nervous high strung women suffer much more than those who are well balanced The fear of the menopause often contributes greatly to the degree of the discomfort

The symptomatology needs little elaboration flushes sweats headaches dizziness exaggeration of nervous instability irritability depression quarrelsomeness There may be mild digestive disturbances and arthralgias are common Objectively the breasts atrophy the external genitalia shrink the vagina becomes drier and the uterus atrophies The change in the vaginal epithelium can be recognized in the vaginal smear Some women exhibit alterations of the electrocardiogram with lowering of the ST segments in all leads especially in lead 2 which promptly disappear after treatment with estrogenic hormone

Severe symptoms occur in about 20 per cent of women Fundamental to all treatment is reassurance of the patient convincing her that the many fears that she harbors concerning the change of life are unfounded Substitution therapy with estrogenic hormone brings rapid relief of symptoms Some gynecologists find that the administration of 0 5 mg of estradiol by mouth three times a day is sufficient Diethylstilbestrol is much cheaper and usually efficacious In some it gives rise to nausea and abdominal pain to such an extent that it cannot be used The average dose is 0 5 mg daily but this has to be adjusted to the needs and the tolerance of the patient If oral administration of these preparations is unsuccessful estradiol benzoate in oil may be given by intramuscular injection Usually 2 000 rat units three times a week is sufficient

There is no physiologic *male climacteric* analogous to the female climacteric Microscopic study shows that in most old men both the germinal and the hormonal function of the testes is preserved The menopause is characterized by a diminished secretion of estrogens and increase in the urinary gonadotrophins In men there is no sudden decrease in androgens although in the later years of life smaller quan

tities of androgens are excreted There is no significant elevation of gonadotrophins in the urine of aging men nor do they suffer from hot flashes or other symptoms of the menopause It is unwise and irrational to administer male hormone to elderly men complaining of weakness or suffering from psychoneuroses

Men of any age who lose testicular function as a result of castration or disease do undergo a climacteric like state As Heller and Myers[3] have shown such men give evidence of testicular failure by an elevation of gonadotrophic substances in the urine and by histologic signs of testicular atrophy or degeneration They exhibit vasomotor psychic and constitutional symptoms similar to those of the female menopause There is loss of libido and of sexual potency Hot flashes are characteristic All of these symptoms are relieved following the intramuscular injection of 25 mg testosterone propionate three to five times a week for two to four weeks The symptoms return when treatment is stopped so that the injections must be continued indefinitely The dosage should be the smallest that will keep the patient symptom free Oral or sublingual administration of the hormone is rarely effective

Differentiation of this genuine male climacteric from psychoneurosis and psychogenic impotence is difficult without estimation of the urinary gonadotrophins or testicular biopsy and these procedures are not adapted to clinical use Hot flashes strongly suggest a true climacteric Often a therapeutic test with injections of testosterone propionate is needed to arrive at a diagnosis If there is no clearcut improvement after two or three weeks of such treatment one should conclude that the symptoms are psychoneurotic and are not caused by loss of testicular function

[3] Heller C G and Myers G B 'The Male Climacteric Its Symptomatology Diagnosis and Treatment J A M A 126 472 Oct 21 1944

After the age of 50 there is a gradual reduction of sexual potency and vigor but there are no accompanying constitutional symptoms By the age of 60 the sexual life of most men is quiescent or past but some retain their sexual powers into the seventh decade One must distinguish between *sexual potency, the ability to have sexual intercourse* and fertility which depends on the presence of motile viable spermatozoa The two conditions do not necessarily go hand in hand Loss of spermatogenesis which is a surer sign of senescence than loss of potency usually manifests itself in the seventh decade, but there are authenticated cases of the birth of children fathered by men of 70 years or older

In spite of depression of gonadal function old men may have a reawakening of sexual activity Prostatic enlargement may by local or reflex irritation, provoke sexual desire and power Often psychological factors the internal and external obstacles to sexual satisfaction may induce masturbation in men in the seventh decade Psychiatrists call this psychosexual regression and find an analogy in the intense concern that many old people show for the functions of their bowels In senile psychoses and dementia sexual aberrations are common All of these manifestations of sexual activity depend on psychological moments, not on activity of the male sex hormone

The treatment with testosterone of sexual impotence and general debility of aging men is rarely indicated It is undesirable even if it were possible to re awaken vigorous sexual activity in an aging organism that may not be strong enough to withstand the strain It is not fortuitous that old men who marry young women often develop coronary thrombosis or die suddenly on their honeymoon or shortly after marriage

Gynecological Conditions

Cystocele cystitis prolapse of the uterus senile vulvovaginitis and tumors constitute the urogenital disorders to which older women are subject

Cystocele and prolapse —These are usually late effects of injuries to the pelvic structures during childbirth They are commonly associated with residual urine in the bladder which may become infected There may be frequent and painful urination or there may be incontinence with dribbling on coughing or laughing Commonly there is an eversion of the urethra and urethral caruncles may form A urethral caruncle is a bright red pea sized sensitive protuberance on the posterior wall of the urethra actually an everted chronically inflamed and congested hypertrophied portion of the urethral mucosa The cystitis may eventually lead to an ascending infection and give rise to pyelitis or pyelonephritis Aside from the urinary tract infection cystocele and prolapse lead to considerable discomfort which usually becomes more distressing with the years as the tissues continue to lose their elasticity and the prolapse becomes more marked

If the patient is in good general condition and if she is in her sixties and still has a considerable expectancy of life operation is the best measure for if well done it will give permanent cure If operation is not feasible a suitable pessary often of the ring type will give relief in many instances Urethral caruncles should be treated by fulguration or by thorough excision of the whole mucosa The urinary infection should be treated with sulfadiazine in doses of 15 gr three or four times a day until the urine becomes clear The same precautions should be observed as when using any of the sulfonamide group of drugs The patient should be kept under observation and frequent blood counts should be made

Senile vulvovaginitis—This results from loss of ovarian activity Following the menopause the uterus tubes and ovaries atrophy The mucous membrane of the vagina and vulva and the skin of the latter become thin, atrophic and fissured The vagina becomes narrowed As a result of lessened secretions these tissues become dry and more susceptible to trauma and infections The early symptoms are pruritis, burning and dyspareunia As a result of scratching excoriations appear At a later stage white thickened wrinkled areas of leukoplakia develop on the vulva In the last stages the dry leathery skin and mucous membrane characteristic of kraurosis vulvae appear

In one third of the cases of leukoplakia carcinomatous metaplasia supervenes Leukoplakia is the most frequent forerunner of cancer of the vulva and occurs on the average, at age 60

Treatment of senile vulvovaginitis with estrogenic hormones is highly successful in the earlier stages of the disease The hormone must be given in sufficient dosage—if by intramuscular injection a total of 50,000 to 100,000 rat units over a period of several weeks Some prefer to use the hormone in the form of vaginal suppositories, and others as an ointment Diethylstilbestrol may be given by mouth in doses from 0 2 to 1 mg daily The dosage by vaginal suppository is 0 5 mg daily There is great individual variation in the amount required It is best to commence with small doses and gradually increase them if necessary When relief has been obtained the smallest dose that will keep the patient symptom free should be continued as the maintenance dose Nausea and vomiting may result from this medication When this occurs the dose should be lowered

The administration of nicotinic acid 50 mg three times a

day, and of vitamin A in the form of cod liver oil seems to aid the recession of the lesions of senile vulvovaginitis

Estrogenic hormone will relieve many of the symptoms of the later stages of senile vulvovaginitis but it will not bring about a recession of the pathological changes of leukoplakia or kraurosis vulvae If symptoms persist or if the lesion suggests that it may undergo malignant change excision of the vulva becomes necessary Some gynecologists advocate excision as a preventive against cancer in every case of leukoplakia but this is probably too extreme a view

Carcinoma of the Body of the Uterus

Cancer of the body of the uterus is encountered on the average at age 55 The presenting symptom is irregular vaginal bleeding occurring after the menopause Physical examination and vaginal inspection with a speculum are negative Diagnosis is made by curettage and pathological examination of the curetted material The lesion is usually an adenocarcinoma In an older woman unexplained bleeding always calls for such a diagnostic curettage Hysterectomy results in a five year survival in 60 per cent of cases and intra uterine application of radium in a five year survival of 55 per cent Most elderly women tolerate hysterectomy well Hysterectomy alone is often followed by recurrence of the tumor in the abdominal and vaginal wounds This is avoided if radium is employed before operation so the best procedure is preliminary intra uterine application of radium followed by hysterectomy This gives promise of 80 per cent five year cures In cases of anaplastic carcinoma operation is ineffective and a combination of radium and x ray therapy is best Technically inoperable cases show a 50 per cent survival after radium and x ray therapy

Carcinoma of the Cervix

Cancer of the cervix is a disease of middle life Less than one third of cases occur after the age of 50 The presenting symptom as a rule is a sanguineous vaginal discharge Examination reveals a hard indurated lesion of the cervix Inspection through the speculum is often less informative than palpation Definitive diagnosis is made by removal of a section of the involved tissue and pathological examination The treatment of choice for most cases is radiotherapy As a rule preliminary roentgen irradiation is used followed by the application of radium In competent hands this leads to five year cures in from 20 to 50 per cent of cases In early localized lesions in young women surgery may be indicated In women over the age of 50 surgical removal is rarely called for

Carcinoma of the Breast

Cancer of the breast constitutes 9 per cent of all cancers and 40 per cent of all cancers in women The average age incidence is 50 one half of all cases occur at ages over 50 The highest mortality occurs between the ages of 55 and 65 Cancer of the breast occurs in males too but is infrequent and develops later in life on the average at age 57 Its pathology and clinical course resemble the disease in women Carcinoma of the breast shows a definite familial incidence

The earliest evidence of cancer of the breast is the discovery of a lump It should no longer be necessary to give the admonition that as soon as a mass has been recognized in the breast a section should be removed for pathological study Only so can cancer of the breast be diagnosed promptly at a time when operation still offers hope of cure The biopsy should be done in the operating room and

immediately examined by the frozen section method so that in case it is malignant the surgeon can at once proceed with the radical operation Whereas in women under 40 85 per cent of mammary lesions examined in the surgical pathology laboratory are benign after the age of 50 85 per cent are malignant The frequency of carcinoma rises rapidly with the years and after age 65 all lesions of the breast are carcinomatous[4]

Not all breast cancers exhibit a rapid growth that leads to early death Of untreated patients 40 per cent are living after three years 20 per cent after five years and 5 per cent after 10 years Metastasis occurs at first to the axillary lymph nodes later to the supraclavicular nodes lungs liver bones and brain By and large the prognosis is better the older the patient Fixation of the tumor but in particular metastasis to the axillary nodes makes the outlook serious Experience of the best clinics has shown that when there is cancerous involvement of the axillary nodes about 25 per cent of patients survive five years after operation If the axillary lymph nodes are found free of metastatic deposits 75 per cent of patients undergoing radical operation are well after five years

These figures emphasize the urgency of early diagnosis and the absolute necessity of including a careful palpation of the breast in every physical examination of a woman The only treatment for cancer of the breast no matter whether the axillary nodes are involved or not is radical operation There are several reasons for this Even when axillary nodes are not palpable microscopic examination may disclose cancerous deposits On the other hand even when axillary nodes are palpable the patient should be given the benefit of the radical operation because microscopic examination

[4] Dawson E K Mammary Cancer and Menopause Edinburgh M J 50 ?71 December 1943

may demonstrate that the adenopathy is inflammatory, not neoplastic Preoperative radiotherapy has been given up by those most experienced in treating cancer of the breast Post operative irradiation is still carried out hopefully by many although the statistical results do not give much encouragement to the premise that such treatment increases the percentage of cures Radiotherapy alone is never indicated except as a palliative measure in certain cases with distant metastases Ovariectomy in women who are still menstruating often leads to absorption and repair of skeletal metastases and orchiectomy in men with metastasizing carcinoma of the breast is said to lead to regression of the primary tumor and of the metastases [5] Large doses of testosterone propionate may bring about regression of the primary lesion and of the metastases The duration of the favorable response has not yet been established

Paget s disease of the nipple —This occurs predominantly in women over 50 years of age The diagnosis should be suspected in the presence of an eczematous lesion of the nipple Commonly scabs form and there is oozing of blood The condition may last for years Diagnosis is made by biopsy and demonstration of epithelial hypertrophy and Pagets cells—clear polygonal cells containing glycogen This is a true malignant lesion which, if untreated will eventually metastasize to the axillary nodes and throughout the body Radical mastectomy is the only treatment

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[5] Treves N *et al* Effects of Orchiectomy on Primary and Metastatic Carcinoma of the Breast" Surg Gynec & Obst 79 589 December 1944

Chapter Fourteen

DISEASES OF THE BONES AND JOINTS, AND GOUT

RHEUMATISM is the most frequent cause of chronic illness and disability among the population of the United States yet it ranks fourteenth as a cause of death It cripples far more than it kills It is estimated on the basis of findings of the National Health Survey that there are some 6 850 000 cases of rheumatism in the United States and some 147 600 persons invalided by their rheumatic condition The frequency of rheumatism increases with each decade up to age 70

The term rheumatism of course has little meaning in the strict medical sense It includes all kinds of disabilities of the bones and joints tendons and fibrous tissues During the past decades some semblance of order has been achieved in grouping the various rheumatic disorders

Osteo Arthritis

Osteo arthritis also known as degenerative or hypertrophic arthritis or osteo arthrosis is the most common disorder of the joints in older persons indeed some degree of osteo arthritis is found in everyone past the age of 50 It

is the end result of a process beginning in youth The natural history of these joint changes has been painstakingly and graphically described by Bennett Waine and Bauer[1] Just as in the case of arteriosclerosis there has been much dispute as to whether osteo arthritis is a disease a result of long continued wear and tear of the joints or a true phenomenon of senescence Apparently all of these factors are concerned in the genesis of the joint changes That aging as such plays a role is shown by the fact that nonarticular cartilages such as those of the trachea epiglottis and ear that are not concerned with weight bearing exhibit with advancing years degenerative processes quite analogous to those in articular cartilages The age at which the degenerative processes in cartilage appear may vary greatly in different individuals some at the age of 30 exhibit changes more advanced than those found in others twice their age and this seems to depend on hereditary endowment Thus constitutional factors determining the tempo of aging play a role Adding their imprint on these basic involutional changes are mechanical factors the endless summation of stresses and strains in the course of daily living The earliest degenerative changes are found at points in the joint that are exposed to maximal pressure and stress weight bearing and use and abuse of joints are important factors Thus the disorder is preponderant in the knees and hips Changes are more extensive on the right side of the body including the right aspect of the vertebral column than on the left Static and other disorders of the joints such as genu valgum or old fractures that interfere with smooth functioning of the joints greatly accelerate the degenerative process

Osteo arthritis is not caused by any known infectious

[1] Bennett G A Waine H and Bauer W *Changes in the Knee Joint at Various Ages* (New York City The Commonwealth Fund 1942)

agents it is not an infectious disease Nor can its cause be found in any disorders of metabolism or of the endocrine glands or in arteriosclerotic impairment of the circulation of the joints Treatment guided by any of these false theories is inefficacious and may be harmful

Osteo arthritis occurs with equal frequency in both sexes Heberden s nodes for some reason are much more common in women than in men The first evidences of osteo arthritis appear quite constantly as early as the second decade The lesions gradually increase with the progress of years and become marked in the seventh decade It is only in the later stages when there has been much destruction of cartilage and hypertrophic lipping of the joint margins that roentgen examination detects the lesion Positive roentgen findings are evident in most persons past the age of 50 but probably less than 5 per cent of these have symptoms Osteo arthritis runs a slow progressive course and although it gives rise to much disability rarely occasions invalidism

The joints that bear the greatest continuous stresses because of the erect posture of man are the ones that most commonly manifest osteo arthritic changes They are the knees the spine the sacro iliac joints and the hip The development of osteo arthritis is favored by obesity which increases the weight borne by the joints and by disturbances of bodily mechanics such as flat feet which cause unequal and irregular weight bearing on the several joint surfaces Certain occupations may induce osteo arthritic changes in individual joints by repeated trauma An example of this is the arthritis of the elbow seen in baseball pitchers Such localized osteo arthritis may follow trauma to a joint it may follow some structural abnormality in and around the joint or it may result from a previous infection of a joint Heberden s nodes which are a common manifestation of general

ized osteo arthritis, seem to be the exception to these general rules It is true that they occur more frequently among laborers than among professional workers, so trauma may play a role, but commonly they develop with no manifest cause

The pathological lesion of osteo arthritis begins as a degenerative process of the articular cartilage at points exposed to maximal mechanical trauma There is a change in the ground substance of the cartilage the cartilage becomes fibrillated and begins to flake off Gradually it becomes increasingly thinner and eventually is worn away The underlying bone proliferates and becomes dense and eburnated Simultaneous with these processes there is active proliferation of new bone around the joint margins This arises both from cartilage and from the periosteum New bone invades the cartilage In this manner the typical hypertrophic changes arise with marginal lipping exostoses and spurs The bone formation at the periphery of the joints arises apparently from the increased stress at the joint margins resulting from weight bearing in consequence of the loss in substance of the articular cartilage The synovial membrane remains normal Ankylosis of the joint rarely results although the new bone formation may lead to considerable limitation of motion

The disease is of slow and insidious development Gradually in the course of months or years the patient complains of increasing pain and difficulty in motion of various joints most frequently the knees the lumbar spine, the lower cervical spine and the hip and rarely the shoulder Heberden's nodes may appear on the fingers The affected joints show little soft tissue swelling although they may be enlarged but there is no redness or fever Creaking and crepitus of the joints are the rule No constitutional symptoms develop There is no loss of weight, no fever no anemia no leukocytosis and no acceleration of the sedimentation rate of the red



Fig 32 — Osteo-arthritis of the knee.



Fig 33 —Osteo arthritis of the spine

blood cells The patient often is much overweight and has weak feet or faulty posture Roentgen examination reveals narrowing of the joint space owing to absorption of the cartilage and irregular spur and lip formation around the joint margins

Localization of the process in the knees is found particularly in obese persons who have static disorders of the feet They complain of pain and stiffness in the knees Stiffness lessens after the joint has been limbered by use but recurs after a night s rest or after sitting a while Crepitus is often felt in the joint Minor strains may lead to sudden painful swelling stiffness and disability that may take weeks to subside

With involvement of the spine pain and stiffness again are the leading symptoms The favorite localization is in the lumbar area The osteophytic process often impinges on the nerve roots as they leave the spine so that radicular pains are common With involvement of the lumbar spine the pain may radiate down the legs When the lesion is higher pain may radiate to the precordium or elsewhere on the trunk There are limitation of motion of the spine and spasm of the paraspinal muscles The roentgen picture shows thinning of the intervertebral disks and bone production along the margins of the vertebrae and at their articulations There is little correspondence between the roentgen picture and the intensity of symptoms Many persons who are entirely free from symptoms have advanced osteo arthritis of the spine as determined by the roentgen ray Others with minimal roentgen lesions have marked disablement Patients with symptoms of osteo-arthritis of the spine often have large pendulous abdomens or breasts the weight of which places a real strain on the vertebral column and contributes to the disturbance

Morbus coxae senilis is osteo-arthritis involving the hip It

occurs after the age of 50 and is usually unilateral Previous trauma or fracture may favor its development The head of the femur is deformed, and there is bone production about the acetabulum so that the head of the femur no longer fits its socket There is a slow onset of pain in the hip joint, with stiffness and resulting limp and limitation of abduction and external rotation Commonly, obturator or sciatic neuralgia results so that the pain is referred to the groin or to the knee Roentgen examination may reveal a narrowed joint cavity exostoses or flattening of the head of the femur

Heberden s nodes are bony exostoses that appear on the proximal ends of the terminal phalanges of the fingers as a result of local periostitis They may develop rather rapidly with local pain and redness of the overlying skin Often light trauma to the affected areas, arising from ordinary use of the hands will bring on swelling redness and pain that last a number of days In other cases, Heberden s nodes may come on insidiously with little pain The patient complains chiefly of the deformity Stecher found Heberden s nodes in almost one quarter of persons between the ages of 50 and 69 and in over one third of those over 70 Heberden s nodes occur chiefly in women There is a distinct familial predisposition to this disorder, but usually only sisters are affected while brothers are free from the disease Inheritance appears to take place only through the mother

Malocclusion of the teeth from faulty natural or artificial dentures causes displacement of the condyle of the mandible and resultant lesions of the temporomandibular joint often with irritation of the auriculotemporal nerve Facial neuralgia tinnitus and headache may result and these can be relieved by appropriate dental reconstruction

Treatment —This is difficult and taxes the patience of both physician and patient If it is intelligently planned and

carried out with persistence good results can be achieved The first indication is to spare the joints that are being damaged by excessive use and by malfunction brought on by static disorders of the body Complete bed rest is rarely essential but the patient should safeguard and rest his joints as much as possible He should not walk too much and if the knees are involved should avoid climbing stairs If there is spondylitis he should avoid bending and lifting if there are Heberden s nodes activities that traumatize the fingers such as heavy housework or manual labor should be eschewed Blows to the fingers by striking the hand carelessly against a hard object often cause an acute inflammatory reaction with subsequent increased growth of the node

Obese patients should lose weight and so lessen the load on the joints Flat feet should be corrected by appropriate appliances a large relaxed abdomen should receive support from a corset a painful spine may need a brace Often the orthopedist must be called on for help At times desiccated thyroid in doses of ½ to 1 gr a day seems to be of assistance The various modalities of physical therapy particularly the several forms of heat and massage are very useful Medication has no effect on the course of the disease but is often needed to relieve pain For this aspirin phenacetin and codeine are the most useful drugs

Rheumatoid Arthritis

Rheumatoid arthritis is the preferred term for the condition also known as infectious or atrophic arthritis It is essentially a disease of the younger years of life Fully 80 per cent of cases have their onset between the ages of 20 and 50 The peak of cases occurs at about age 35 The disease runs a prolonged course and many patients survive into the sixth decade or longer Individual cases may have their onset in the

later years of life I have seen a typical case that made its first appearance in the patient's eighty fifth year Rheumatoid arthritis is three times as common in women as in men Although it is probably an infectious disease, the causal organism has not been identified For many years it was believed that foci of infection in the teeth tonsils prostate or gallbladder were the cause This view has been relinquished even by its former most ardent advocates after hundreds of patients have been operated on and mutilated without benefit

The initial pathological lesion is an inflammation of the synovial membrane which becomes thickened by exudative and proliferative processes Swelling and inflammation extend to the periarticular tissues The proliferating synovial tissue grows over the articular cartilage invades and gradually destroys it When opposing surfaces of joint cartilage are covered by this pannus of inflamed granulation tissue adhesions form The end stage is marked by fibrous or bony ankylosis and subluxation of the joints

The onset may be sudden with acute swelling redness and painfulness of several joints and high fever There is usually symmetrical joint involvement More often the onset is not so stormy but is marked rather by an insidious indolent inflammation of many joints in slow succession Any joint may be involved but the joints of the fingers the wrists and the knees are the favorite localizations Muscle atrophy in the regions around the joints and trophic disorders of the skin of the extremities quickly develop Thickening of the periarticular tissues with atrophy of the muscles above and below the joint gives the part its typical spindle shaped appearance The skin becomes shiny and smooth red or dusky purplish and there may be trophic disturbances of the nails Systemic manifestations are fever, loss of weight secondary anemia and a rapid sedimentation rate of the red blood cells

The lymph nodes draining the affected joints are often enlarged Subcutaneous nodules are found in one fifth of the cases They occur over bony prominences—the olecranon the sacro iliac joints the spinous processes—and may persist for years Valvular heart disease indistinguishable from rheumatic heart disease is a frequent complication especially at younger ages

Roentgen examination at first reveals no changes in the contours of the joint surfaces only swelling of the soft tissues and decalcification of the bones In the later stages of the disease as a result of destruction of the articular cartilage the joint spaces become narrowed and punched out areas may appear in the bones near the joint surfaces In the final stage there are bone production and ankylosis

Unlike rheumatic fever the disease does not have a self limited course with restoration of the joints to normal The arthritic manifestations last for weeks or months vary in intensity shift from one joint to another and usually leave some permanent joint deformity Eventually contractures and subluxations result The constitutional symptoms persist too The patient loses weight progressively and may become quite emaciated and anemic The sedimentation rate of the red blood cells is one of the best indicators of continued activity of the infectious process Until it reaches normal figures the disease is not arrested Even when the disease is completely quiescent one cannot speak of cure for recurrences are common There may be free intervals of months or years but as a rule sooner or later the arthritis again lights up

Treatment —During the active stage of the arthritis rest in bed is essential The bed should be firm and the mattress should not sag Every effort should be made to maintain the nutrition of the patient and to combat the wasting that commonly occurs The diet should have a high caloric value and

should contain a full complement of the accessory foodstuffs If the patient is anemic repeated blood transfusions are indicated Iron is not helpful until the infectious stage has passed Joints that are acutely inflamed should be immobilized in light splints but these splints should be removed daily and the joints should be subjected to gentle passive motion to prevent ankylosis Codeine or salicylates are given to relieve pain but have no effect on the course of the disease As the acute stage subsides various forms of physiotherapy may be employed Heat often gives great relief An infra red lamp may be used 30 minutes once a day or an electric pad or a baking apparatus If the patient can be moved without too much pain hot baths for 20 to 30 minutes once a day at temperatures between 95 and 102 F often give great relief Diathermy or short wave treatments are sometimes helpful At times heat in any form increases the pain in the joint In such cases it should not be used until the lesion has become more quiescent Gentle massage and passive movements of the joints should be carried out immediately after heat treatments

Every effort should be made to prevent contractures and deformities If ankylosis develops the joint should be immobilized in its optimum functional position The knee joint for instance should be fully extended not flexed the elbow on the other hand should be flexed at about 90 degrees When the disease has become quiescent certain deformities may be corrected by operation

Nonspecific protein therapy is helpful in some cases This may be given in the form of boiled skim milk 5 cc intramuscularly every day or every other day Intravenous injection of typhoid vaccine is more effective Such injections often give rise to chills or more severe reactions and should not be employed in patients who are too old or who have

arteriosclerosis of the coronary cerebral or peripheral arteries The initial dose of typhoid vaccine is usually 10 000 000 organisms The dose is increased by about 50 000 000 with each successive injection The succeeding injection is given 24 hours after the febrile reaction to the previous injection has worn off

Gold seems to be establishing itself as a valuable therapeutic agent in rheumatoid arthritis Its use is still in the experimental stage and serious toxic reactions occur in 20 per cent of cases The reader who wishes to employ it is advised to consult the most recent authoritative literature

Removal of foci of infection is no longer the center of all therapeutic endeavor in cases of rheumatoid arthritis In rare instances a recently inflamed solitary joint will clear up after extraction of an infected tooth but as a rule removal of foci of infection has no effect on the course of the disease I have seen a serious exacerbation of symptoms following tonsillectomy or wholesale tooth extraction Infected teeth or other structures in the body that give rise to local symptoms should be treated or removed with a view to relieving the local condition not with the hope of curing a systemic rheumatic infection Thus in a patient with repeated attacks of tonsillitis and enlarged tonsillar lymph nodes tonsillectomy is indicated whether or not he has rheumatoid arthritis

No direct effect of climate on rheumatoid arthritis has been demonstrated but the disease is less frequent in tropical and semitropical regions Certainly these patients feel better if they can escape the northern winters for a sojourn in the south

FIBROSITIS

Fibrositis is a term applied to an ill defined syndrome embracing a variety of conditions characterized by aches and

pains in muscle and fibrous tissues The laity speaks of muscular rheumatism Pain stiffness and soreness appear suddenly in a muscle around a joint or in a fascial sheath There is no fever or constitutional reaction The pain is worse in the morning after a nights immobility and gradually lessens with use of the affected structures The physical findings consist of tenderness over the affected area at times some muscle spasm and occasionally fibrous nodules These nodules occur most often over the sacro iliac joints or in the occipital region at the base of the skull In the latter region these nodules may cause severe headache sometimes called nodular headache caused by involvement of the great occipital nerve Lumbago is fibrositis of the lower part of the back

The symptoms may be exceedingly acute causing complete disability for a few days or they may be milder but persistent The patient complains of a dull ache aggravated by movement The parts involved are stiff and there may be muscle spasm The pain commonly shifts from one part of the body to another Exposure to cold and wet and to drafts often precipitates acute episodes of pain These patients are very sensitive to changes in weather, and on dull rainy days their pains are apt to be worse

The cause of fibrositis is unknown Rarely infected sinuses or other foci seem to be responsible for the symptoms Although the condition causes much annoyance and occasional acute suffering it is not a progressive disease Symptoms often recur, but permanent disability does not result

Treatment —This is concerned primarily with general hygienic measures to keep the patient in good general condition Exposure to wet or to sudden changes of temperature should be avoided The diet should be adequate the bowels regulated The patient should avoid fatigue and obtain enough sleep In the acute stage, rest is the best measure

The affected part should be warmly wrapped to protect it against chilling and drafts Aspirin phenacetin or codeine given in suitable doses controls pain Counterirritation with plasters oil of wintergreen or surface heat lessens the pain Within a few days when the acute symptoms lessen heat and massage give great relief These measures can be employed at once in subacute and chronic cases Diathermy radiant heat and vigorous massage are the best measures Massage is often very painful at first particularly over nodular areas but if persisted in hastens recovery Injection of a 1 per cent solution of procaine hydrochloride into the several tender areas of the involved structures is a useful procedure Areas painful to digital pressure are carefully mapped out A small quantity of procaine is injected into the skin over the site of the lesion the needle is then inserted until it reaches the tender spot and 3 cc of the solution is infiltrated Following the injection the patient should be encouraged to move and use the part freely One injection often gives instant and lasting relief At times it may have to be repeated

Periarthritis of the Shoulder

Periarthritis of the shoulder or subdeltoid bursitis is not restricted to the aged but is commonly seen in men over the age of 50 It is usually associated with injury to the supraspinatus tendon or with calcium deposits in the tendinous cuff that forms the capsule of the shoulder Bosworth in a roentgen study of the shoulders of some 6 000 supposedly normal persons found calcification in these tendons in 2 7 per cent of all cases Most of his patients were under the age of 40 but incidence of calcification increased with each decade after 40 Only 34 per cent of persons with calcifications had symptoms Painful shoulders may be without calcifica

tion Tenosynovitis of the long head of the biceps and its sheath is another cause of painful shoulder

The cause of symptoms is not fully understood The condition is not related to any form of arthritis Trauma seems to be of great importance The original lesion in the supraspinatus tendon may be due to excessive strain subsequently, sudden wrenching of the shoulder may cause the chalky deposits to initiate an acute irritative reaction

The shoulder syndrome may appear suddenly with intense pain and immobilization of the joint As the acute symptoms subside the shoulder remains painful some motion returns but abduction and external rotation are sharply limited Pressure on the tendon of the long head of the biceps may elicit pain There is tenderness on pressure over the shoulder particularly over its upper and outer aspect and the patient cannot lie comfortably Sleep may be interfered with for weeks Atrophy of the muscles around the shoulder and trophic disturbances of the hand commonly follow Roentgen examination often reveals calcified deposits in the region of the supraspinatus tendon These subacute symptoms may develop insidiously without a previous acute stage

There is a curious and frequent association of this shoulder affection and angina pectoris With rare exceptions the left shoulder is involved when there is left sided radiation of anginal pain the right shoulder when there is right sided radiation Commonly the shoulder disability comes on acutely immediately following a coronary thrombosis

Treatment —In the acute stage complete rest and immobilization with wet dressings are the best treatment If there is no perceptible improvement within a few days aspiration

[2] Boas E P and Levy H "Extracardiac Determinants of Site and Radiation of Pain in Angina Pectoris with Special Reference to Shoulder Pain" Am Heart J 14 540 November 1937

of the bursa and injection with 5 to 10 cc of procaine solution or irrigation of the bursa and washing out of calcified deposits may give quick relief Roentgen therapy may bring about rapid subsidence of symptoms[3] A single treatment with a dose of 300 r is often sufficient but treatments may have to be repeated Commonly there is an aggravation of symptoms during the first day with rapid relief from pain and recovery of mobility of the shoulder within 48 hours Roentgen treatment is less useful in chronic cases for it benefits only one third of them Diathermy helps at times but often gives little relief and it may intensify the symptoms Massage should also be employed In older patients the symptoms may persist for months and cause great suffering Often codeine must be given to permit sleep In time there is complete recovery Frequently the calcified deposits eventually become absorbed

Night Cramps

Sudden severe painful cramps in the muscles of the calf are common in elderly persons They usually come at night awaken the patient from sleep last from a few to 15 minutes and commonly recur during the night The spastic contracted muscle is tender and tenderness persists even after the cramp has passed The patient finds relief by getting up by massaging the affected part and by applying heat Their cause is unknown but they occur chiefly in persons who have arthritic changes in the hips or knee joints They are unrelated to circulatory disturbances in the legs The blood calcium and phosphorus levels are normal and the administration of calcium does not appear to be useful Three

[3] Brewer A A and Zink O C Radiation Therapy of Acute Subdeltoid Bursitis J A M A 122 800 July 17 1943

to 5 gr of quinine taken on retiring by blocking the myo*neural junction successfully prevents these cramps Night cramps may disappear spontaneously for weeks or months,* but usually recur

Dupuytren s Contracture

Contracture of the palmar fascia occurs not infrequently with advancing age Its cause is unknown Certain cases seem to bear a relationship to coronary artery disease with angina pectoris particularly when there is associated peri arthritis of the shoulder Apparently neurogenic trophic dis turbances may be concerned in its genesis *As a rule the con dition is bilateral. There is no pain The slow progressive contracture of the palmar fascia draws the fingers particu larly the fourth and fifth into a permanent position of flexion* Treatment is ineffectual and attempts at surgical correction usually fail

Osteoporosis

With advancing years the bones undergo involutional changes It is unknown to what extent these are phenomena *of normal senescence or to what degree they result from di etary faults or other factors* The average *American* diet is grossly *insufficient* in calcium *and it is quite probable* that this calcium lack accentuated by the passage of years leads to the demineralization of bones that is so characteristic of aged persons In addition there may be poor absorption of calcium resulting from derangements of digestion of the aged The end result is osteoporosis with atrophy of the bony cortex a looser internal architecture and an increasing coarse ness of the mesh of the bony trabeculae *Added to this* or in *dependently there is osteomalacia a loss of calcium with softening of the bones* There may be irregular new bone pro duction but the new bone is free from calcium Roentgen

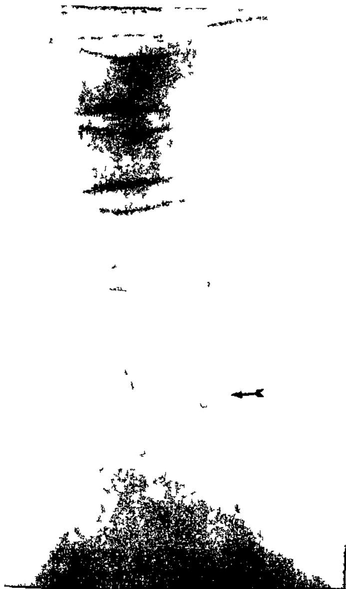


Fig 34 —Senile osteoporosis with compression fracture of the fourth lumbar vertebra

examination reveals the altered structure of the bone as well as its decalcification

As a result of these alterations of bony structure and composition fractures occur more readily most commonly in the spine They are encountered beginning with the seventh decade Low back pain in an elderly person commonly is due to a compression fracture of one or more vertebrae often brought on by minimal trauma In acute cases there may be severe pain and immobility of the back and the development of kyphosis with shortening in stature Any form of low back pain in the aged calls for roentgen examination of the spine which will often reveal a compression fracture Such fractures may be accidental findings in the course of a roentgen examination for another purpose In the lumbar region the intervertebral disks may herniate into the bodies of the softened vertebrae A compression fracture of an osteoporotic spine should be distinguished from one due to metastatic neoplasm A possible primary neoplasm should be searched for The finding of a normal sedimentation rate of the red blood cells and normal values for serum phosphatase helps to exclude the presence of neoplasm

Treatment involves support of the spine with a suitable brace that does not immobilize the patient, a diet rich in calcium and supplementary administration of calcium and vitamin D Milk is the best source of calcium, and 1 qt should be taken daily In addition calcium should be given in the form of 4 Gm of calcium gluconate or 3 Gm of calcium lactate three times a day Vitamin D is best given in the form of cod liver oil

Postmenopausal osteoporosis is a condition occurring almost exclusively in women who have had a natural or artificial menopause, and is characterized by deficient calcium

deposits in the osteoid tissue[4] It is a disorder of the bone matrix not of calcium metabolism The calcium and phosphorus contents of the blood are normal but calcium excretion in the urine is increased The serum phosphatase level is not elevated There may be kidney stones due to the increased excretion of calcium

The spine and pelvis are chiefly involved The symptomatology is characteristic A middle aged woman who has passed through the menopause complains of localized pain in the back following a relatively minor jolt or trauma Roentgen examination discloses a fractured or collapsed vertebra and rarefaction of the bodies of the vertebrae and the pelvic bones

These patients respond well to treatment with estrogenic hormone Although there is no primary disturbance in calcium metabolism it is well to give plenty of calcium in the daily diet—a quart of milk or its equivalent—and vitamin D

Paget's Disease

Paget's disease is a rare condition occurring with equal frequency in men and women past 50 It is characterized by enlargement and thickening of the bones There are fibrosis of the marrow irregular bone absorption and much endosteal and periosteal new bone formation which undergoes irregular calcification Most of the bones of the body may be involved or the process may be restricted to a few bones especially the sacrum pelvis and spine The serum calcium and phosphorus levels are normal but the serum alkaline phosphatase is much increased (normal is 4–12 King Armstrong units) more than in hyperparathyroidism of similar

[4] Albright F Smith P H and Richardson A M "Postmenopausal Osteoporosis" J A M A 116 2465 May 31 1941



Fig 35 —Paget s disease of the skull



FIG 36 —Paget s disease of the legs

extent The disease is not caused by altered function of the parathyroid glands

The patient first complains of pain and weakness of the legs The tibiae become thickened but because of their weakened structure they undergo bowing with the convexity forward from the weight of the body Subsequently the femora become involved and thickened and bent with an outward convexity Marked kyphosis of the spine develops the chest becomes rigid and breathing becomes largely abdominal The patient grows shorter and his head grows larger Deafness may result from involvement of the petrous portion of the temporal bone, impairment of vision from narrowing of the optic foramina These changes develop very slowly and may remain localized to just a few bones Spontaneous fractures are common rarely, osteogenic sarcoma develops The disease does not shorten life nor cause death Generalized arteriosclerosis is present in all cases and recurrent bronchitis is very common owing to the immobility of the chest

The roentgen picture is quite characteristic The skull is enlarged and greatly thickened and has a moth eaten appearance The bones have a thickened cortex are poor in calcium, the normal architecture is largely lost, and they present a spongelike appearance which is due to an irregularity in the distribution of the calcification

In half the cases Paget s disease gives rise to no symptoms and is an incidental finding discovered in the course of roentgen studies for other complaints

There is no effective treatment of Paget s disease Injections of parathormone or of dihydrotachysterol may relieve the bone pains that are often distressing

Metastatic Neoplasm of the Bones

Bony metastasis is common to many different neoplasms It occurs with particular frequency in cancers of the breast prostate thyroid and lungs At times the metastatic lesion gives rise to the very first symptoms of disease and may lead to a pathological fracture or to the erroneous diagnosis of arthritis Thus a man aged 52 complained of severe pain and limitation of motion of the left hip and of a mild cough There were clinical signs of an acute lesion of the hip joint some abnormal physical signs in one lung and a roentgenogram disclosed a neoplasm of the lung Bronchoscopy verified the diagnosis and roentgen examination of the hip showed metastatic deposits around the hip joint Another man complained for months of severe pain in the lower thoracic spine The lower spine was tender and rigid There were no other physical signs of disease and the roentgen picture of the spine was normal The pain continued and gradually secondary anemia developed The sedimentation rate of the red blood cells was persistently rapid Months later the diagnosis of carcinoma of the pancreas with metastasis to the spine was finally made

When an older person develops severe bone or joint pain and no other cause is evident metastatic carcinoma should always be thought of Often the roentgen examination discloses the nature of the lesion but at times the roentgen changes may be greatly delayed A persistently rapid sedimentation rate of the red blood cells elevation of the serum alkaline phosphatase low fever the development of anemia or at times the finding of abnormal white cells in the stained blood smear should suggest the diagnosis Then a thorough search should be made for the primary lesion Marked increase in serum acid phosphatase is corroborating evidence

Treatment can never be curative but great symptomatic relief often follows high voltage roentgen radiation of the bones involved by the neoplastic process

Multiple Myeloma

Multiple myeloma occurs on the average at age 55 and is three times as common in men as in women[5] It is a neoplasm arising in the bone marrow and invading the bony cortex made up of typical myeloma or plasma cells Pathologic fractures often occur and may give rise to the first symptoms of disease Compression fractures of the spine are particularly frequent and radicular pains are common Many bones are involved especially the ribs spine and skull

The presenting symptom usually is severe bone pain most often in the thorax or the lumbar region of the spine There is tenderness over the affected areas of bone Secondary anemia becomes marked with great weakness and progressive loss in weight Eventually cachexia develops and uremia is a common terminal event Bence Jones protein is found in the urine in about half the cases There is an increase in both total serum protein and serum globulin contents an association found in few other conditions This is probably responsible for the greatly accelerated sedimentation rate of the erythrocytes and of the tendency of the red blood cells to form rouleaux Abnormalities of the white blood cells are less common but immature cells of the myeloid series and plasma cells may be found in the blood smear The blood calcium content is usually normal but may be elevated the alkaline phosphatase content is normal

Diagnosis rests on discovery of Bence Jones protein in the

[5] Bayrd E D and Heck F J Multiple Myeloma J A M A 133 14 1947

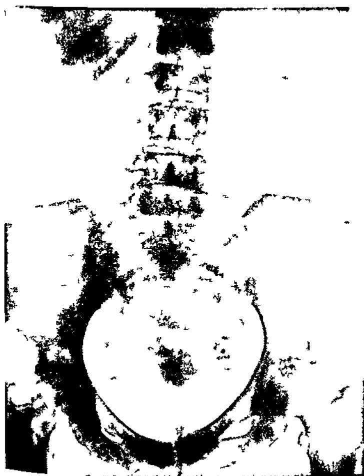


FIG 37 —Diffuse bone metastasis secondary to carcinoma of the breast

urine and of myeloma cells in aspirated sternal marrow Roentgen examination reveals typical punched out areas in the bones especially the skull ribs and spine There is no curative treatment Roentgen therapy may relieve bone pains Recent reports indicate that a series of 15 intravenous injections of 150 mg of stilbamidine combined with a diet low in animal proteins may relieve pain and lead to considerable temporary improvement[6]

Gout

Gout is a metabolic disturbance the true nature of which is not yet understood For the present we have grouped it with disorders of the joints because its chief manifestations are arthritic and these are often confused with other diseases of the joints Gout constitutes 5 per cent of all cases of arthritis It is characterized by an increase of the uric acid in the blood serum by its familial incidence by arthritis and by deposition of urate tophi in the joints bursae tendons and subcutaneous tissues In normal persons the level of uric acid in the serum never rises above 5 mg per cent The gouty person has serum uric acid figures between 6 and 14 mg per cent High serum uric acid values are found in relatives of persons with clinical gout who may have no other manifestations of the disease Similarly high uric acid levels may be encountered in the gouty person long before he has clinical evidences of gout In this sense we may speak of a gouty diathesis a familial disorder of uric acid metabolism that underlies and precedes the clinical manifestations of gout Such a gouty diathesis can be discovered only by chemical examination of the blood and recognition that the

[6] Snapper I "Stilbamidine and Pentamidine in Multiple Myeloma" J.A.M.A., 133 157 1947

individual in question belongs to a gouty family The loose use of the term gouty diathesis and the habit of stigmatizing as gouty patients with arteriosclerosis contracted kidneys psoriasis eczema or migraine have no basis in fact and lead only to fuzzy thinking and incorrect diagnoses

It seems probable that a person without the inborn disturbance of uric acid metabolism will not develop gout but the nature of the dyscrasia is still unsolved The ancient idea that gout results from overeating and abuse of alcohol must be discarded Talbott[7] has shown that gouty patients when on a purine free low protein diet may have acute attacks as frequently as when their food intake is unrestricted But there are factors that precipitate acute attacks of gouty arthritis and among these are excessive banqueting and drinking Some patients discover that the ingestion of some particular article of food will lead to an attack Injury to a joint or even a mild strain such as that provoked by a long hike or participation in active sport may act as the trigger mechanism An intercurrent infection or a surgical operation commonly brings on acute gout At times attacks are precipitated by injections of liver extract or of a mercurial diuretic

Gout is encountered in two forms—acute gouty arthritis an acute inflammation of one or more joints with constitutional manifestations and chronic gouty arthritis chronic joint changes resulting from repeated attacks of acute arthritis with deposition of tophi and permanent joint deformities Acute gouty arthritis first makes its appearance in the fourth and fifth decades but many cases are encountered in older persons Chronic joint changes develop about 10 to 15 years after the onset of gout so that chronic gouty arthritis

Talbott J H Gout (New York City Oxford University Press 1943)

is seen chiefly after the age of 50 Fully 95 per cent of cases occur in males

In the early years of the disease the pathological changes are restricted to microscopic deposits of urate crystals in the articular cartilages of the affected joints It is this precipitation of urates that is supposed to initiate the acute inflammatory attack of arthritis Gradually through the course of years and following many acute attacks the urate deposits increase and may completely cover the articular cartilage In time the cartilage is destroyed and replaced by urate deposits which may collect in masses forming tophi These changes of the articular surfaces together with the irritative effect of the urate deposits cause a proliferative reaction of the synovial membrane and joint capsule as well as joint and bone changes similar to those seen in osteo arthritis Tophi become deposited in the epiphyseal bone giving rise to the punched out areas visible on the roentgen film In the course of time tophi form in bursae tendons the cartilages of the ears and subcutaneous tissues They may ulcerate when they become very large

The kidneys almost always become affected The earliest findings are urate deposits in the kidney parenchyma In the course of time there is progressive destruction of glomeruli and tubules usually ending with the final picture of primary arteriolar contracted kidney To what extent the pathogenesis of this lesion is related to the urate deposits and to what extent to the hypertension and arteriosclerosis that so commonly accompany gout is unknown Uric acid stones are frequently formed and there may be pyelonephritis

Generalized arteriosclerosis and in particular coronary artery sclerosis are quite constant in advanced cases

Acute gouty arthritis appears suddenly usually between the ages of 35 and 40 More often than not the patient is

awakened from sleep by intense pain in one joint most frequently the metatarsophalangeal joint of the great toe By morning the joint is swollen, tense hot red and exquisitely tender There are fever and leukocytosis The great toe is involved in 50 per cent of cases but the process may be localized in the ankle, knee or wrist The shoulders hips and spine are rarely affected If untreated the acute inflammation lasts from three to ten days usually with nightly exacerbations of pain In the early stages of the disease tophi are rarely found With subsidence of the acute inflammatory reaction the joint returns to normal and the patient may feel better than ever Within a year or so there is a second attack and following this the seizures come with gradually increasing frequency

Chronic gouty arthritis becomes manifest after many years of recurrent attacks of acute gout In time the inflammation of the joint does not completely subside some stiffness pain and deformity remain and there are acute exacerbations at varying intervals It is at this stage that tophi appear in the helix and antihelix of the ear in the tendons or in the subcutaneous tissue around the joints The olecranon or prepatellar bursae become thickened and filled with urates Albumin and casts are found in the urine and very gradually evidences of impairment of kidney function appear marked at first by lowered specific gravity of the urine and lack of concentrating power of the kidneys Finally there may be kidney insufficiency and eventual death from azotemia Uric acid calculi may form and there may be attacks of renal colic Arteriosclerosis and hypertension with any of their secondary manifestations are common

Diagnosis —Acute monarticular arthritis, developing suddenly particularly at night in a man aged 40 or over should always arouse the suspicion of gout If the great toe is in

volved the diagnosis is practically certain Characteristic too is the fact that the attack subsides in about a week with complete restoration of the joint to normal If the patient is seen after he has had a number of attacks the history is of the utmost importance The story of repeated attacks of intense monarticular arthritis with a complete remission between at tacks is encountered in no other condition The development of arthritis after one of the known precipitating causes of gout is suggestive Acute arthritis following operation is almost invariably gouty The diagnosis of chronic gout is often revealed by the discovery of tophi in the cartilages of the ears or elsewhere or thickened olecranon or prepatellar bur sae A history of former attacks of acute arthritis with com plete remissions is very suggestive Elevation of uric acid in the blood serum to 6 mg per cent or more confirms the diag nosis The therapeutic test with colchicine is of great value for gouty arthritis alone promptly responds to treatment with this drug Roentgen studies of the joints may be of as sistance The characteristic finding in chronic gout is sharply demarcated punched out areas in the bone around the joints Material scraped from a tophus and studied under the micro scope will show urate crystals Such a finding is diagnostic

The older the patient at the onset of symptoms of gout the better the prognosis A patient who has his first attack of arthritis after age 50 does not develop serious pathological lesions Although the underlying gouty disorder of metabo lism cannot be cured the condition can in large measure be held in check by appropriate treatment

Treatment —If the patient is seen in the acute attack he should be put to bed and the affected joint protected by a cradle Hot moist compresses are often soothing Codeine or morphine may have to be given for the pain A saline ca thartic such as magnesium sulfate 1 oz , should be given at

once Colchicine is a specific for acute gouty arthritis, although its mode of action is unknown The active principle is better than the tincture or the wine of colchicum Colchicine is administered by mouth in tablets of 1/100 gr Two tablets should be given at once and following this 1 tablet should be given every two hours until either nausea or diarrhea becomes manifest With the onset of such symptoms the drug should be stopped Relief from pain and diminution of swelling of the joint occur within 24 hours, as a rule During the acute attack large amounts of fluids should be taken The diet should be free from purines and low in fats and should consist of milk eggs hominy or farina potatoes fruits and vegetables such as tomatoes, string beans, cabbage carrots and beets [8]

When the attack is over treatment should be continued to prevent recurrent arthritis and the development of chronic gouty arthritis and cardiovascular and renal complications In spite of the fact that some authors believe that dietary control has no influence on the course of gout it seems wiser until we know more about the nature of the disorder to keep the diet free from purines two days a week and low in purines on the other days The fat intake should be low, the carbohydrate allowance liberal Protein should be derived largely from milk cheese and eggs Iron and vitamin B complex should be added to the diet Coffee and tea may be taken but alcohol should be avoided

Some patients learn to recognize symptoms of an impending attack such as twinges of pain in a joint, polyuria suppression of sweating or gastro intestinal disturbances In such cases, a saline cathartic and several doses of colchicine 1/100 gr every few hours may abort the attack If a gouty

[8] Hench P S "Diagnosis and Treatment of Gout and Gouty Arthritis J A M A 116 453 Feb 8 1941

patient contracts an infection or is compelled to undergo operation the taking of colchicine 1/100 gr three times a day may prevent an attack of gout Some authors advise long-continued intermittent administration of colchicine to patients with severe progressive gout In chronic gout and in cases with persistent elevation of the blood uric acid level certain drugs that augment uric acid excretion by the kidneys

TABLE 6 — PURINE FREE DIET

Foods allowed

Fruits of all kinds in liberal amounts
Vegetables except asparagus beans kale mushrooms peas spinach
Bread and cereals fine cereals like farina and white bread in limited amounts Avoid oatmeal whole grain cereals whole wheat bread
Dairy products butter cheese cream milk eggs
Coffee tea cocoa in small amounts

Foods prohibited

All meats fish poultry game

SAMPLE MENU

BREAKFAST	LUNCHEON
Fruit or fruit juice	Cheese eggs or cereal
Farina or rice with cream and sugar	Vegetable salad
Eggs	White bread and butter
White bread and butter	Fruit
Milk	Milk

DINNER

Cream vegetable soup	Fruit or rice pudding
Cheese or egg dish	Crackers and butter
Vegetable potato	Milk

should be given Cinchophen is the most effective of these but in view of the fact that it may cause acute hepatitis and jaundice it should not be used unless all other measures fail The salicylates too increase the elimination of uric acid Sixty grains of aspirin should be given daily for four consecutive days of every week With this enough alkali should be given to keep the urine alkaline and so prevent the pre

cipitation of urates in the urine and formation of uric acid gravel or stones Fifteen to 30 gr of potassium citrate or 30 to 60 gr of sodium bicarbonate should be given three times a day The patient should be taught to test his urine with litmus paper and to take enough alkali to keep the urine alkaline Two to 3 qt of fluids should be taken daily

If cinchophen must be used it should be given in a dosage of 7½ gr three times a day for three consecutive days every week The patient should be instructed to report promptly the development of itching of the skin and nausea or other gastro intestinal symptoms If any such symptoms arise, the drug must be stopped immediately Fatal liver degeneration may result in persons who are sensitive to cinchophen

Tophi that become very large or that ulcerate should be excised [9]

With consistent careful treatment acute attacks of gout can be avoided and the development of chronic gouty arthritis and of the chronic visceral manifestations of gout can be prevented

Fractures of the Neck of the Femur

Fracture through the neck of the femur is a common accident in older persons, one that is attended with grave hazards In former years the ensuing prolonged immobility in bed brought with it a mortality of 75 per cent Laplace[10] reported on 500 fractures of all sorts excepting skull fractures Most of them were hip fractures Of the patients over 80 52 per cent died of those between 70 and 79 35 per cent, of those between 60 and 69, 23 per cent died, and of those

[9] Linton R R and Talbott J H "Surgical Treatment of Tophaceous Gout" Ann Surg 117 161 February 1943

[10] Laplace L B "Cardiovascular Complications of Fracture" Am J Surg 44 161 1939

under 60 2 per cent died An associated cardiovascular condition added greatly to the gravity of the prognosis Death usually occurred after the first or second week of immobilization and was caused by peripheral circulatory failure (see p 66) The dangers of prolonged bed rest for patients with fractures of the neck of the femur are becoming well recognized Tinker[11] found that with conservative treatment only 51 per cent of these patients achieved bony union and 25 per cent died With operative fixation of the fragments bony union occurred in 78 per cent and the mortality was only 9 per cent A study of the results of operative treatment by members of the American Academy of Orthopedic Surgeons showed bony union in 88 per cent and a mortality of 8 5 per cent[12] These figures give telling evidence of the superiority of operative treatment Operative fixation of the fragments by a nail or similar device and application of an appropriate ambulatory splint within a few days enables the patient to be up and about within a short time and eliminates the hazards of prolonged bed rest

Many patients can be operated on shortly after the accident If there is shock it may be necessary to wait a day or two until this has passed General anesthesia with cyclopropane or ether is usually well borne Spinal anesthesia may be used in appropriate cases The common postoperative complications in the order of frequency are infection pulmonary involvement—pneumonia or infarction decubitus ulcers heart failure and coronary thrombosis

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[11] Tinker M B and Tinker M B Jr Fracture of the Neck of the Femur J A M A 112 791 1939

[12] Am. Acad Orthopedic Surg "Treatment of Fractures of the Neck of the Femur by Internal Fixation" J Bone & Joint Surg 21 485 1939

Chapter Fifteen

INFECTIOUS DISEASES

INFECTIONS OF THE RESPIRATORY TRACT AND EARS

ACUTE tonsillitis is uncommon in the aged and chronic infections of the tonsil are infrequent as shown by the rarity with which enlarged tonsillar lymph nodes at the angle of the mandible are encountered Tonsillar tissue diminishes steadily after the sixth decade but rarely disappears completely[1] In 5 per cent of persons over age 60 the tonsils are large In the old as in the young the tonsils are rarely foci of infection that give rise to constitutional disorders The arthritides arthralgias and myalgias are not relieved by tonsillectomy, indeed this operation is seldom indicated in the aged

Elderly persons are by no means immune to colds and mild upper respiratory infections, but sinusitis is less common and as a rule milder than in the young Coryza frequently leads to bronchitis and bronchitis to bronchopneumonia Thus every cold should be taken seriously Bed rest and the maintenance of an equable constant temperature in the room are the most important therapeutic measures If the nasal discharge or the bronchial secretions become purulent or if the bronchitis is more than minimal, it is wise to institute im

[1] Kelemen G Clinical Observations on the Palatine Tonsil in the Aged Ann Otol Rhin & Laryng 54 421 June 1945

mediate treatment with sulfonamides or penicillin to prevent more serious complications such as pneumonia

Suppurative otitis media is uncommon in the later decades of life Of 1 514 cases of suppurative otitis media only 2 per cent occurred in persons over the age of 60[2] But in these older patients the course of the disease was much more severe Sixty eight per cent of those between 60 and 69 and 86 per cent of those between 70 and 79 developed mastoiditis requiring surgical intervention The evolution of such mastoiditis may be very insidious in older persons particularly when the infecting organism is pneumococcus type III It is wise to obtain early cultures of the pus from infected ears to treat such patients vigorously with sulfonamides or penicillin and to keep them under close observation

Pneumonia

From 6 to 7 per cent of all deaths between the ages of 50 and 80 are caused by influenza and the pneumonias The death rates remain fairly constant for each succeeding decade old age does not bring with it a greater chance of dying from pneumonia But an older person who contracts pneumonia incurs a much greater hazard than a young person for mortality rapidly mounts with increasing age

Lobar pneumonia is relatively infrequent among older persons Of 1 867 cases of pneumococcus pneumonia studied by Cecil Baldwin and Larsen only 8 7 per cent occurred in persons aged 60 and over As in the younger age groups pneumococcus types I II and III are responsible for fully two thirds of the cases With advancing years there is a lessening in the occurrence of types I and II and an in

[2] Rosenwasser H Infections in the Nasal Accessory Sinuses and the Ears in Old Age Arch Otolaryngol 41 18_ March 1945

increasing incidence of type III The Friedlander bacillus which is responsible for about 4 per cent of all pneumonias invades almost exclusively persons past middle age and it tacks males seven times as often as females

Lobar pneumonia may have the same clinical course in elderly persons as in the young In the aged and in those greatly debilitated by some chronic disease it may exhibit such atypical symptomatology that it may not be recognized The patient may just become confused or stuporous and may develop weakness or paralysis of one side of the body In such cases the sclerotic cerebral arteries do not supply enough blood to the brain when toxemia impairs the efficiency of the circulation Signs and symptoms may be latent the patient may be up and about and die suddenly, and the pneumonia may be first discovered at autopsy

Usually there is no initial chill no chest pain and little febrile reaction The patient may have had a slight cold and becomes greatly prostrated for no apparent reason He may complain of headache or may become delirious In other cases the onset is marked by vomiting or diarrhea and progressive weakness There is little cough and no expectoration The temperature may barely reach 100 F and leukocytosis may be slight The distinctive feature that should always arouse suspicion of pneumonia is an increase in the respiratory rate Examination may reveal widespread consolidation of the lungs, out of proportion to the constitutional reaction When there is much pulmonary emphysema the physical signs of consolidation may be few and appear late There may be no dullness and the development of bronchial breathing is delayed Defervescence is often by lysis The mortality of lobar pneumonia is high among older patients and increases with each decade Pneumococcic endocarditis and meningitis are not uncommon complications

Bronchopneumonia is a disease of infancy and old age The majority of pneumonias in older persons are bronchopneumonias In over 85 per cent of pneumococcus bronchopneumonias types IV to XXXII are the causative organisms Types I II and III are rarely encountered Many other bacteria may give rise to bronchopneumonia It is a common terminal infection in cachectic patients and in those debilitated by disease It occurs frequently in patients with pulmonary emphysema and as a sequel to an attack of bronchitis Aspiration pneumonia develops when because of impairment of the glottal reflex mucus and bacteria from the nose and throat are drawn into the lungs This occurs during anesthesia coma or with advanced debility If septic organisms from the teeth or from ulcerating carcinomas of the mouth or upper air passages are aspirated a necrotizing pneumonia or lung abscess results Atelectatic pneumonia a term to be preferred to hypostatic pneumonia occurs when bronchi become plugged with mucus Atelectatic areas are produced and these readily become infected Prolonged bed rest particularly when the patient is too weak to change position commonly induces atelectatic pneumonia Plaster casts that inhibit the respiratory excursions of the thorax act in a similar manner

Bronchopneumonia usually develops insidiously It is marked by an increased respiratory rate variable cough some febrile reaction and toxemia Toxemia is manifested by weakness mental confusion and delirium The physical findings may be scanty Usually there is some dullness at one or both bases posteriorly with diminished breath sounds and moist sticky rales in both lower lobes Bronchial breathing is usually absent In patients with advanced heart disease it is difficult to distinguish between pulmonary infarcts and bronchopneumonia Both conditions come on insidiously and give

rise to similar symptoms and physical signs Autopsy studies often indicate that what was interpreted as bronchopneumonia in a patient with advanced chronic heart failure actually was a pulmonary infarct

Pneumonia in the elderly patient commonly follows a head cold or other upper respiratory infection The aged should take special measures to avoid such infections and in particular should isolate themselves from friends and relatives who are suffering from colds and coughs They should avoid going out in inclement weather and exposure to drafts Persons who are particularly susceptible to winter colds do well in a southern climate They should avoid large populous centers like Miami where fresh infections are brought in daily by the thousands of visitors from the North and settle in a small, quiet community To avoid pneumonia every effort should be made to prevent old people from becoming bedridden. When they are confined to bed, their position should be constantly changed and they should be propped up as much as possible Plaster casts that immobilize the chest should be avoided Codeine and morphine should be used sparingly for they suppress the cough reflex and favor the development of atelectatic pneumonia Recent studies hold out some promise of successful prophylactic vaccination against pneumonia Kaufman[3] has reported vaccination of several thousand inmates of the New York City Home with a capsular antigenic polysaccharide Among the vaccinated group in two successive winters there were only one-quarter as many cases of pneumonia as in the nonvaccinated controls If these observations are confirmed, vaccination may prove a valuable measure against upper respiratory infection in susceptible persons and a prophylactic against postoperative pneumonia.

[3] Kaufman P "Studies on Old Age Pneumonia," Arch Int Med. 67 304 February 1941

Treatment—If treated early the pneumonias of older persons respond well to the sulfonamide drugs and to penicillin Chemotherapy has greatly brightened the outlook in this serious infection of the aged which formerly brought with it a mortality of over 50 per cent The first element in successful treatment is early diagnosis If pneumonia is recognized within 24 hours of its onset it usually responds promptly to chemotherapeutic treatment

The general treatment of pneumonia corresponds to that given pneumonia patients irrespective of age The fluid intake should be liberal and the diet light Oxygen is administered if there is much cyanosis or labored breathing These aging patients have not the endurance of younger patients and should be spared every unnecessary strain Supportive treatment of the heart is often necessary In the young we no longer give digitalis routinely in case of pneumonia But in the elderly and aged who so often have some complicating cardiovascular disease or who have advanced pulmonary emphysema which increases the work of the right heart digitalis is often helpful and at times life saving In the presence of hypertension and advanced coronary sclerosis or of pulmonary emphysema digitalis should be given If the patient has not been taking digitalis 1½ gr should be given three times a day for the first three days and after that twice a day for another week

Enough codeine morphine or other sedatives may be used to ease the cough and allay restlessness but as mentioned previously extreme caution is necessary in using these drugs

Erysipelas

Erysipelas is more common in persons of advanced years than in persons in the younger age groups Old people are

apt to become careless about the cleanliness of their bodies their skin is dry and atrophic and minor abrasions and cracks of the skin occur and are easily overlooked with resultant infection Debilitating chronic diseases diminish resistance to infection Two thirds of the cases start on the face the rest mostly on the legs Often the clinical course resembles that seen in younger patients but in many instances just as in the case of the pneumonias the disease comes on insidiously without great febrile reaction The mortality in the past has been high over 40 per cent Since the introduction of the sulfonamides the outlook has been greatly improved As soon as the diagnosis has been made 2 to 4 Gm of the drug should be given immediately Then 1 Gm should be given every three hours day and night Usually the temperature drops and the progress of the lesion is arrested within 24 hours The dosage should be continued at 1 Gm every four hours for another day or two until it is certain that the infection is clearing up It may be well if there is appreciable residual infection to continue with 1 Gm two or three times daily for a few days longer Penicillin is equally effective Exposure of the affected area to ultraviolet radiation usually arrests the progress of the lesion within 24 to 48 hours

Syphilis

This is no place for a detailed discussion of syphilis and its complex symptomatology Syphilis is a disease of youth and even its tertiary and neurological manifestations develop for the most part before the age of 50 If patients with syphilis survive beyond the sixth decade, their symptoms and the indications for their treatment do not differ from those of the younger age groups Cardiovascular syphilis is discussed in Chapter 7 Primary or secondary syphilis oc-

curring in older persons runs the same course as in the young and calls for the same treatment

General paresis —About 10 per cent of paretics admitted for the first time to state hospitals in New York State are over the age of 60 Four times as many males as females are admitted The incubation period of paresis is the shorter the older the patient when infected Therefore in paretics 60 years of age or older the primary infection has taken place either a long time ago (40 or 50 years) or recently (within five to seven years) The symptoms are those of an organic psychosis with no distinguishing characteristics There are impaired memory and judgment senile deterioration with delusional trends The neurological signs are difficult to distinguish from those of cerebral arteriosclerosis The Argyll Robertson pupil is by no means constant The blood Wassermann reaction is negative in about 30 per cent of cases in contradistinction to the invariable positive reaction in the younger age groups The Wassermann reaction and the colloidal gold curve of the spinal fluid are positive This indicates the need for examination of the spinal fluid of all older psychotic patients to avoid missing the diagnosis [4]

Latent syphilis —The chief problem that arises in older persons is posed by the discovery of a positive Wassermann reaction in an individual with no signs or symptoms of syphilis —the syndrome of so called latent syphilis The diagnosis of latent syphilis should not be made lightly The patient should be subjected to a painstaking physical examination with particular attention to the cardiovascular and nervous systems In every case a spinal tap should be made and a complete examination of the spinal fluid including particularly the cell count the Wassermann reaction and the colloidal gold

[4] Arieti S General Paresis in Senility Am J Psychiat 101 585 March 1945

test should be carried out If there is evidence of visceral syphilis or if the spinal fluid shows a positive reaction the case should not be classed as one of latent syphilis and active treatment should be given Only if the spinal fluid is normal and there are no physical signs of organic disease due to syphilis should the diagnosis of latent syphilis be made

Latent syphilis encountered less than four years after the initial infection calls for continuous active treatment as given for early syphilis The management of latent syphilis discovered more than four years after the initial lesion should be individualized If the patient is so old that his life expectancy is only 10 to 15 years the hazards of treatment with arsenicals may be greater than the risk of the development of syphilitic lesions Moreover there is such a thing as spontaneous cure of syphilis and arrest of the disease is not uncommon As a rule if latent syphilis is accidentally discovered in a person over the age of 60 it is wisest to withhold treatment unless a full course of penicillin is given as outlined below It is particularly dangerous to give a few casual injections of arsenic or bismuth to such patients for this may disturb the immunity relations between the spirochete and the body and stir up the disease

If the spinal fluid reaction is negative in a patient with latent syphilis at least four years after the initial infection there is no need to worry about the possible subsequent development of neurosyphilis it practically never occurs But if the spinal fluid gives any indication of syphilis even if the patient is asymptomatic and the blood Wassermann reaction is negative active treatment must be instituted because in these cases there is grave danger of the future development of neurosyphilis Such patients should be treated as are those with neurosyphilis at younger ages and this in

volves the use of tryparsamide and of fever therapy if the simpler methods do not bring results

In a patient over the age of 60 with evidences of visceral or cerebrospinal syphilis enough treatment should be given to bring about symptomatic relief it should not be pushed as vigorously as in a younger person Tabes dorsalis may be arrested and inactive in a patient past 60 In such cases treatment may be unnecessary and inadvisable

The treatment of syphilis and of neurosyphilis is in a state of flux pending evaluation of penicillin therapy Preliminary reports indicate that penicillin will be a most valuable aid in the treatment of latent syphilis and of neurosyphilis Final opinion on the optimal dosage has not crystallized The average course of treatment for neurosyphilis is 80 000 units intramuscularly every three hours day and night for 7½ days or a total of 4 800 000 units[5] Such dosage may be repeated one or two times if there is no appreciable improvement but this is rarely necessary Most of the improvement occurs in the first four months but may continue to become manifest for a year or more A favorable change in the spinal fluid occurs in about 74 per cent and normal spinal fluids result in 36 per cent Clinical improvement is observed in 65 per cent of patients with symptomatic neurosyphilis and in 30 per cent of those with paresis or with tabes dorsalis In asymptomatic neurosyphilis penicillin is more effective than any other measure in reducing the spinal fluid to normal Such treatment would appear to be suitable for latent syphilis as well

The old line therapy for latent syphilis involves three courses of eight intramuscular injections of 3 gr of bismuth in oil alternating with three courses of eight intravenous in

[5] Stokes J H and Steiger H P "Penicillin Alone in Neurosyphilis" J A M A 131 1 May 4 1946

jections of neoarsphenamine During the following two years the patient should receive each year two courses of 12 injections of bismuth No attempt should be made to push treatment to achieve a reversal of the positive Wassermann reaction This often cannot be accomplished in these late cases and is clinically unimportant

Chapter Sixteen

DIABETES

DIABETES has become a problem of middle age and of the later years of life It is estimated that there are 500 000 diabetics in the United States[1] Of these one quarter are under the age of 50 one quarter are between 50 and 60 and one half are over the age of 60 Yet only one ninth of the population is over 60 years old The age specific prevalence rates of diabetes rise steadily with the years the rate of increase is accelerated after age 50 up to age 75 when the incidence again drops Diabetes occurs more frequently among women particularly after age 50 The diabetic population is increasing more rapidly than the general population because of the increasing numbers of old people and of women in the population The onset of the disease occurs under age 50 in one fourth of the cases between the ages of 50 and 64 in one half and over age 64 in one quarter The average age at onset is 54 years As a result of modern methods of treatment diabetics are spared death from coma and survive to die in their later years from some complication In older persons diabetes appears in a milder form and many older diabetics have had the disease for years The average duration of life

[1] Spiegelman M and Marks H H "Age and Sex Variations in the Prevalence and Onset of Diabetes Mellitus" Am J Pub Health 36 26 January 1946

when diabetes has had its onset at age 50 is 14 years, at age 60 it is 10 years, and at age 65 it is 8 years The average age at death is about 64 years and most diabetic deaths occur during the seventh decade of life

The causes of death of diabetics have undergone a radical change during the past 40 years Today the cardiovascular renal diseases are the leading causes accounting according to Joslin s figures for some 60 per cent of deaths Breaking down this figure further, we find that cardiac disorders account for 30 per cent cerebral vascular insults for 11 per cent and gangrene of the extremities for 4 per cent of deaths The average age at death from an arteriosclerotic complication is 68 years Cancer is responsible for about 8 per cent and tuberculosis for about 4 per cent of deaths

In the old as in the young hereditary influences and obesity favor development of the disease

In elderly persons the onset of diabetes is usually insidious Most often it is evidenced by polyuria loss of weight and pruritus vulvae Commonly it is discovered by routine urine examination of a patient who comes to the physician with another complaint Arteriosclerotic heart disease or peripheral vascular disease often brings the unrecognized elderly diabetic to the physician Hypertension is encountered in fully one half of all older diabetics

Management

General treatment of the elderly diabetic corresponds to that of younger diabetics The urine must be kept sugar free and the weight of the patient held within average normal figures In recent years there has been an *increasing* tendency to give more sugar and less fat in the average diet This seems particularly important in older patients because

of the apparent relationship between fat and cholesterol metabolism and atherosclerosis The average dietary should contain in the neighborhood of 150 Gm of carbohydrates 80 Gm of proteins and 100 Gm of fat Exercise increases the sugar tolerance of diabetics and all patients should be encouraged to engage in moderate physical activity up to their capacity The older the patient the more slowly should treatment be instituted It is not wise to make an elderly patient undergo strict starvation at the onset of treatment in an endeavor quickly to free his urine from sugar and reduce the level of sugar in the blood Such radical treatment favors the development of thromboses in the coronary cerebral or peripheral arteries It is much better to proceed slowly and to allow several weeks for establishment of proper dietary adjustment and for elimination of glycosuria and hyperglycemia

In many old patients mild diabetes can be controlled without insulin If glycosuria does not yield to dietary measures alone and if the patient continues to lose weight insulin should be given Most cases can be controlled with an appropriate dose of protamine zinc insulin For details, the reader should consult any of the diabetic handbooks

Special care should be taken to avoid insulin overdosage and shock because in older persons hypoglycemia often leads to vascular accidents in the domain of the cerebral coronary or peripheral arteries Insulin administration should be preceded by careful dietary control over a period of time, so that the approximate insulin needs of the patient can be estimated The initial dose of insulin should be small and the amount gradually increased If protamine zinc insulin is used it is well to give a small feeding before bedtime to avoid a hypoglycemic reaction during the night

A major part of the treatment of the elderly diabetic con

cerns itself with the prevention early recognition and therapy of complications

Arteriosclerosis develops with much greater frequency and at younger ages in diabetics than in the population at large Men and women are affected alike so that diabetic women in contrast to women without this disorder have arteriosclerosis of the coronary cerebral and peripheral arteries as commonly as do diabetic men

Arteriosclerosis of the coronary arteries giving rise to the syndromes of angina pectoris and cardiac infarction is a major problem in elderly diabetics The treatment of this heart condition in diabetics does not differ from that of patients with normal sugar metabolism The diabetes should be treated conservatively Although the urine should be kept free from sugar no rigorous attempts should be made to reduce the blood sugar levels to normal figures These patients do not stand too rigid dieting and do best on a diet containing about 150 Gm of carbohydrate Too great restriction of carbohydrate may result in frequent anginal attacks which cease when the diet is again made more liberal Protamine zinc insulin or regular insulin may be used freely in these patients but sudden large increases in dosage should be avoided and great care should be taken to avoid hypoglycemia and hypoglycemic shock Such an event may induce cardiac infarction

Peripheral arteriosclerosis is almost universal in long standing diabetes Calcification of arteries can be demonstrated in 90 per cent of patients who have had diabetes for 10 years or more This is true even in the young Arterial occlusion with resultant gangrene is common and its frequency increases with age The average age at onset is 64 Gangrene develops predominantly during the winter months Prevention of gangrene and infection of the lower extremities

involves the same principles that have been outlined in the discussion of peripheral arteriosclerosis (p 136) There must be scrupulous cleanliness of the feet and avoidance of trauma The feet should be kept warm in cold weather The diabetes too should be well controlled If dry gangrene develops conservative treatment is indicated These patients have a short life expectancy and amputation involves a serious hazard Often it reduces them to a state of invalidism and they never learn to walk with an artificial limb Commonly gangrene in the other leg starts soon after amputation of the one first affected Many of these patients may come through with only the loss of all or a part of a toe if they are treated with infinite patience and meticulous care The patient should be kept in bed for activity of the muscles greatly increases their need for blood and the narrowed arteries cannot admit enough flow to supply the muscles as well as the feet The feet should be kept below heart level so that the force of gravity may aid in the flow of blood to the extremity The foot should be protected by a cradle dressings as a rule are unnecessary The application of heat is dangerous unless the temperature is rigidly controlled If the temperature is too high the local metabolism of the tissues is increased and this calls for more blood than the diseased arteries can supply Pain often results and there may be an extension of tissue destruction If the temperature is too low it may induce vasospasms and further impair the local circulation The temperature of the extremity should be kept constant at 92 F by means of a thermostatically controlled heating device in the cradle The only operative procedure permissible is simple drainage if necessary proximal to the inflammatory area of the zone of demarcation One should wait until spontaneous sloughing takes place and this may take weeks or months

When there is moist gangrene the situation becomes much more urgent for then there is active infection of the tissues Wet dressings should be applied and full doses of sulfadiazine or penicillin given The diabetes should be carefully watched for with such infection the diabetes rapidly becomes more severe and acidosis readily occurs The carbohydrate intake and the amount of insulin should be increased If the infection does not show prompt signs of recession early amputation should be undertaken

Before amputation careful studies of the arterial circulation of the leg should be made The oscillometer and studies of skin temperatures give the best information Amputation should be done below or above the knee depending on circumstances Lower amputations are rarely indicated Anesthesia is best given by the spinal route Treatment of the diabetes immediately before and after operation corresponds to that outlined subsequently for all operations or infections

Furuncles and *carbuncles* constitute serious complications The patient should at once receive full doses of sulfadiazine or penicillin Radiotherapy should be given to the carbuncle simultaneously If the carbuncle continues to develop despite treatment and if the diabetes begins to get out of control operation with excision of the carbuncle may become necessary Carbuncles are frequently followed by cortical abscesses of the kidneys and by perinephric abscess This contingency should always be kept in mind

Pneumonia complicating diabetes is treated as it is in other patients

In the presence of *intercurrent infection* whether it be carbuncle pneumonia an infection of the leg or of the kidney adjustment of the diet and of insulin must be made The diet should contain a liberal portion of carbohydrates and should consist of milk cereal cream and eggs The urine should be

examined every few hours Insulin is given every three or four hours in a dosage adjusted to the amount of sugar in the urine Regular insulin should be used A rough and ready guide is the color of the Benedict solution after reduction If the color is red give 20 units of insulin if it is orange give 15 units if yellow 10 units and if yellowish green 5 units When the infection has subsided and the temperature has returned to normal the regular diabetic diet with appropriate insulin dosage can be resumed

Operation and anesthesia induce a serious disturbance of carbohydrate metabolism probably by damaging liver function in particular the storage of glycogen Before operation the patient should receive from 150 to 200 Gm of carbohydrate a day for several days and enough insulin to assure its utilization In case of an emergency operation it is well to give 100 Gm of carbohydrate intravenously before proceeding Following operation at least 150 Gm of carbohydrate should be given daily intravenously if necessary On the morning of operation one half to two thirds of the usual dose of protamine zinc insulin should be given and this may be continued after operation if the intake of carbohydrate is kept adequate After operation crystalline insulin should be given every four hours in dosage determined by the urinary reaction for sugar in the same manner as is done in case of infections Spinal anesthesia and ethylene seem to be the anesthetics of choice for diabetics General anesthetics often cause serious disturbance of liver function and so interfere with carbohydrate metabolism by preventing storage of glycogen in the liver One third of all operations on diabetics are amputations The operative mortality is about 11 per cent Carbuncles have an operative mortality of 9 per cent

Infections of the urinary tract are common in diabetics Autopsy studies reveal that about 20 per cent of persons

dying of diabetes have infection of the kidneys. Cortical abscesses of the kidneys have been mentioned. Ascending infections of the urinary tract are of frequent occurrence, particularly when there is some obstruction in the urinary tract. Such infections may be asymptomatic and discoverable only by finding bacteria and pus in the urine. They may suddenly light up and give rise to a severe necrotizing pyelonephritis. An unexplained increase in the severity of the diabetes always calls for investigation of the urinary tract. Patients with prostatic enlargement should be handled with particular care. Catheterization should be avoided unless absolutely necessary and then should be carried out with meticulous asepsis. Just as in nondiabetics urinary infections are often controlled by the administration of sulfadiazine 1 Gm. four times a day, or of streptomycin. The diabetes should be treated vigorously and plenty of fluid should be given. As soon as possible a complete investigation of the urinary tract should be undertaken.

Intercapillary glomerulosclerosis is the name given to a characteristic glomerular lesion found in approximately two thirds of all diabetics at autopsy, especially in those over the age of 40.[2] There is a focal or diffuse fibrosis of the glomeruli with scattered typical spherical hyaline lesions. Similar lesions occur in about 12 per cent of patients with subacute or chronic glomerulonephritis but otherwise are rarely encountered in nondiabetics. The development of the lesion bears no relationship to the degree or duration of the diabetes nor is it necessarily accompanied by hypertension, albuminuria, renal insufficiency or edema. Kimmelstiel and Wilson,[3]

Laipply, T. C., *et al*. "Intercapillary Glomerulosclerosis." Arch. Int. Med. 74:354, 1944.

[3] Kimmelstiel, P., and Wilson, C.: Intercapillary Lesions in the Glomeruli of the Kidney. Am. J. Path. 12:83, November 1936.

in their original description associated a distinct clinical syndrome with the lesion namely diabetes marked albuminuria extensive edema and frequently hypertension and renal insufficiency More recent studies show that only 6 per cent of persons in whom intercapillary glomerulosclerosis is found at autopsy show this clinical picture When it occurs the syndrome runs the course of the nephrotic stage of chronic glomerulonephritis with a poor prognosis

Gall stones occur with particular frequency in diabetics Joslin reports that at autopsy gall stones are found in fully [illegible]5 per cent of diabetics as contrasted with at most 10 per cent in nondiabetics Many of these patients have no symptoms of gallbladder disease When symptoms do occur they usually antedate the diabetes by about five years It is a moot question whether chronic gallbladder infection can cause diabetes but it certainly can make it more active Gallbladder disease in diabetics is dangerous because complications such as cholecystitis and cholangitis are not only serious in themselves but may induce an increase in severity of the diabetes Operation for gallbladder complications in diabetics carries a mortality of some 10 per cent It is wise therefore to remove a gallbladder containing stones from a diabetic as soon as it is recognized before more serious complications may develop

When *appendicitis* occurs in a diabetic the onset is apt to be insidious and the symptoms atypical They may simulate diabetic coma Appendicitis carries an operative mortality of 10 per cent in diabetics Lowering of this rate depends on constant alertness and vigilance on the part of physicians

Cancer occurs not infrequently in diabetics Curiously enough cancer of the pancreas is especially common comprising fully 10 per cent of all cancers encountered in diabetics It does not seem to aggravate the severity of the diabetes

Tuberculosis occurs with sufficient frequency in diabetics to make it necessary to look for it in every patient with pulmonary symptoms or unexplained fever In such cases a roentgen film of the chest and a sputum examination are indispensable The presence of diabetes accelerates the course of pulmonary tuberculosis unless the diabetes is vigorously treated

Cataracts of the senile type are common in elderly diabetics and may require operation Initial treatment of diabetes is often associated with a reduction of near vision The cause of this hyperopia is not fully understood but it seems to depend on changes in refraction of the lens It disappears when the diabetes is brought fully under control In the interim the patient may have to wear spectacles with plus 3 lenses Tobacco amblyopia seems to be more common in diabetics than in persons with normal sugar metabolism A diabetic who complains of disturbances of vision should give up smoking

The nature of so called *diabetic retinitis* is not yet clearly understood Diabetic retinitis is characterized by tiny punctate hemorrhages and deep lying circular punctate exudates with sharp margins usually distributed around the macular region The retinal veins may be dilated and there may be nodular dilatations and constrictions of the veins which are usually associated with large areas of hemorrhage There may be hemorrhage into the vitreous and subsequent scar formation and detachment of the retina The retinal lesions bear no relationship to the severity of the diabetes nor to the degree of care with which it has been treated but they are uncommon in cases of less than three years duration Diabetic retinitis may develop in the absence of hypertension or vascular disease It can be distinguished from hypertensive retinitis whose features are flamelike hemorrhages and fuzzy

cotton wool exudates When the two conditions occur simultaneously it may be difficult to differentiate one from the other The prognosis of diabetic retinitis is better than that of retinitis associated with hypertension Vision usually remains good unless the macula is involved Wagener and his associates[4] encountered diabetic retinitis in 17 7 per cent of 1 052 cases of diabetes It occurred chiefly in patients over the age of 40 and was often accompanied by hypertension In 25 per cent it was associated with diabetic neuropathy

Diabetic neuropathy occurs in patients with neglected and poorly treated diabetes In them it may be precipitated by an intercurrent infection an operation or a bout of diabetic coma Neuropathy occurs as often in mild as in severe cases of diabetes It is caused apparently by a basic metabolic disturbance induced by the diabetes and not by a vitamin B deficiency[5] The neuropathy may involve not alone the peripheral sensory and motor neurons but elements of the autonomic nervous system concerned with intestinal bladder and vasomotor functions Early symptoms are usually manifested in the lower extremities and are characterized by muscular weakness pains and cramps worse at night and on exposure to cold The tendon reflexes may be diminished or absent and there may be diminution of cutaneous sensations and of vibratory sense Muscle tenderness is common Impairment of peripheral sympathetic nerve supply may give rise to sweating deficiencies loss of vasomotor control and dependent edema and trophic disorders of the skin The pupils may be sluggish small irregular and unequal Anorexia nausea obstinate constipation or constipation with alternating diarrhea may occur Im

[4] Wagener H P et al "Retinitis in Diabetes" New England J Med 211 1131 1934

[5] Rundles R W "Diabetic Neuropathy" Medicine 24 111 May 1945

potence and true atonic bladder paralysis are not uncommon Orthostatic hypotension has been observed The spinal fluid often shows moderate elevation of total protein which in severe cases may rise to levels as high as 400 mg per cent

The diffuse nerve lesions and the abnormality of the spinal fluid indicate that diabetic neuropathy is caused by a systemic disorder namely the disturbed metabolism of long standing unregulated diabetes This view is confirmed by the fact that the only effective treatment consists of strict regulation of the diabetes and the use of insulin The administration of vitamins is of no benefit Early diagnosis is important, for if promptly and adequately treated the neuropathic changes are reversible

Chapter Seventeen

DISEASES OF THE THYROID GLAND

Hyperthyroidism

HYPERTHYROIDISM in the aged does not manifest the classic symptoms of exophthalmic goiter and consequently is often overlooked An unexplained loss of weight or a rapid pulse rate in an older person should always arouse the suspicion of hyperthyroidism Indeed these may be the only symptoms Usually marked asthenia sleeplessness and increased nervousness are also present Commonly the patient does not present the marked motor restlessness that is so characteristic of younger patients Some are so quiet and depressed that the condition has been designated the apathetic type of hyperthyroidism Enlargement of the thyroid gland and abnormal eye signs are commonly lacking

These patients present themselves to the physician in various guises One group complains of loss of weight and weakness Often the appetite is poor in contrast to the usual increased food consumption by patients with Graves s disease The patient appears wasted maybe even cachetic and naturally the suspicion of carcinoma is aroused The distinctive feature that should always suggest hyperthyroidism is the rapid pulse rate ranging between 100 and 120 Yet there are some patients whose pulse rates never exceed 80 At times

auricular fibrillation may lead to the correct diagnosis The blood cholesterol is usually low Careful inquiry into the *symptomatology will usually reveal increased nervousness* and insomnia some shakiness of the hands a tendency to diarrhea and intolerance of heat

More rarely abdominal symptoms dominate the clinical picture There may be persistent nausea vomiting and abdominal pain More commonly diarrhea manifests itself This may be so severe as to suggest the existence of ulcerative colitis Again the rapid pulse rate and marked *loss of weight* should direct attention to the thyroid gland The diagnosis is *confirmed if gastro intestinal studies are negative* and a basal metabolic rate determination reveals an elevated metabolism

Usually a cardiac symptomatology is so much in the foreground that the patient is suspected of having some primary form of organic heart disease The absence of thyroid enlargement of abnormal eye signs and maybe of tremor makes it easy to overlook a thyroid disorder The patient complains *of dyspnea and palpitation He* has lost weight and may give a history of nervousness and diarrhea He may be intolerant of hot surroundings On examination the only significant finding may be a heart rate between 100 and 140 or auricular fibrillation with a rapid ventricular rate Auricular fibrillation in the absence of demonstrable organic *heart* disease in older people should always arouse the suspicion of *hyperthyroidism The following case may serve* as a typical example

A man aged 60 for two years had had increasing weakness dyspnea on exertion and palpitation For one month the symptoms had been worse His weight one year before was 195 lb his present weight 155 lb He was a serene well built man The eyes were not prominent The thyroid gland was not palpable and no substernal struma was *visible on the roentgen film The lungs were emphysematous,* with

some rales at the right base The heart was not enlarged the sounds were rather faint and there were no murmurs The rhythm was absolutely irregular with a ventricular rate of 150 The electrocardiogram showed auricular fibrillation The blood pressure was 140 80 mm The radial and temporal arteries were sclerotic It was thought that the patient had auricular fibrillation associated with arteriosclerosis There was no other evident etiological factor Digitalis was administered Twenty-one cubic centimeters of the tincture was given in three days yet the ventricular rate was 120 In the first nine days of treatment 16 cc of the tincture was administered there was no nausea or big miny and the ventricular rate did not fall below 90 In the subsequent seven days 39 cc more of tincture of digitalis was given with no further drop in pulse rate The unexplained resistance to the effects of digitalis led to estimation of the patient s basal metabolic rate This was plus 54 on one occasion and plus 65 on another

Cardiac symptoms in hyperthyroidism are conditioned by various physiological disturbances of the circulation which serve to increase the work of the heart to such an extent that cardiac enlargement and eventually heart failure may ensue The factors increasing the work of the heart are the increased metabolism necessitating an increased minute volume flow of blood an increased blood velocity and an increased blood volume and the direct effect of the thyroid secretion on the heart When there is pre existing heart disease cardiac disability develops much more rapidly Congestive failure occurs chiefly in patients with some form of organic heart disease The extra load superimposed by the thyroid disturbance overtaxes the heart whose reserve is already impaired

Because of the high incidence of cardiac disorders in older people cardiac complications occur much more frequently in older individuals with hyperthyroidism than in the young In the earlier stages before serious damage to the heart has developed the symptoms are those arising from an overactive

heart and an unstable vasomotor mechanism registered by a hypersensitive nervous system The patient complains of palpitation pulsations in the neck head and epigastrium and shortness of breath The pulse rate is rapid and is little slowed by rest or sleep The heart may or may not be enlarged Enlargement is more common in older individuals and in those with auricular fibrillation The first heart sound is sharp and snapping and may simulate the one heard in mitral stenosis The electrocardiogram is not characteristic The systolic blood pressure is usually elevated from 10 to 30 mm Hg and is extremely labile If the diastolic pressure is over 95 there is a concomitant essential hypertension

Auricular fibrillation occurs during the course of hyperthyroidism in about 20 per cent of all cases Its incidence is much greater in the older age groups At first it is paroxysmal in its appearance The attack may last minutes hours or days and between the paroxysms the rhythm of the heart is regular The patient experiences marked palpitation and some dyspnea during the attack but characteristically is not nearly as disabled as the patient with auricular fibrillation associated with mitral stenosis or hypertension In spite of a rapid ventricular rate he usually walks about with little cardiac distress and without evidence of congestive heart failure In the course of time the irregularity comes on more and more frequently and the duration of the attacks is longer, until finally auricular fibrillation becomes permanently established Even at this time heart failure occurs only in very long standing cases or when there are complicating cardiac lesions Auricular fibrillation of hyperthyroidism is marked by rapid ventricular rates Another characteristic is the resistance of the ventricular rate to slowing by digitalis Exceptionally large doses must be given to achieve this effect and such doses are tolerated without the appearance of toxic

symptoms This large tolerance for digitalis may at times have diagnostic value disclosing on further investigation an occult case of hyperthyroidism

When hyperthyroidism is superimposed on valvular or hypertensive heart disease its recognition is still more difficult Tachycardia out of proportion to the cardiac lesion an unexplained auricular fibrillation or loss of weight should lead the physician to check the patient s basal metabolic rate The added strain imposed by the hyperthyroidism may in such cases give rise to serious cardiac symptoms Patients with enlarged hearts may develop heart failure and those with coronary arteriosclerosis may experience frequent anginal attacks

Treatment —As in the young successful treatment usually calls for operation Older persons resist the idea of operation and of course they do present a greater operative risk When ever restoration of health by subtotal thyroidectomy seems possible surgical intervention is the treatment of choice If the patient refuses medical treatment is instituted The patient should be put to bed and given a high caloric diet He should be relieved of as many cares and responsibilities as possible Three to five drops of Lugol s solution should be given once a day Sedatives such as phenobarbital should be freely administered If the patient gains weight and if the pulse rate slows and the basal metabolic rate drops the patient may gradually be allowed more liberties However the iodine medication and a modified rest cure should be continued for six to twelve months for the arrest of active hyperthyroidism is a slow process and cure is rare Exacerbations of symptoms may occur at any time even during careful treatment

Thiouracil is useful in the treatment of some older persons for whom operation is not feasible Thiouracil leads

to a fall in oxygen consumption and in basal metabolic rate by inhibiting the production of thyroid hormone The thyroid gland becomes hyperplastic but contains no colloid As a result of the administration of thiouracil the symptoms of thyroid intoxication disappear within a few weeks and remain in abeyance as long as the drug is given Thiouracil does not cure hyperthyroidism for when its administration is stopped excess hormone is again produced and the original symptoms recur However hyperthyroidism has a cyclic course and spontaneous remissions occur It may be possible to give the drug until such a spontaneous remission takes place It is not without danger for a few fatalities from agranulocytosis have been reported The dosage is 0 2 Gm two or three times a day for four weeks then 0 2 Gm daily for six months White blood cell counts should be made twice a week to detect the earliest evidence of granulopenia If the white cell count drops appreciably the drug should be stopped at once Some patients develop a transient rash or fever This is not of serious import and does not call for stopping the drug

Subtotal thyroidectomy is the treatment of choice because it offers the most favorable prospect for quick and permanent cure An added indication in patients with adenomatous goiter is the danger with advancing years of malignant degeneration of the gland With meticulous preoperative preparation and skillful operation the risk is small Preparation for operation consists of bed rest and the administration of a high caloric diet and 10 drops of Lugol s solution three times a day Sedatives should be given as needed Preoperative care may take one week or many weeks Most patients can be brought to an optimum condition within two weeks But operation should never be hurried A favorable response is evident in a gain in weight and a reduction of pulse rate

and basal metabolic rate A drop of metabolic rate to plus 30 or below indicates that it is safe to operate If the patient does not respond to preoperative treatment operation should be postponed In borderline cases the two stage operation should be performed in order to maintain complete control

The presence of a cardiac complication whether it be simple enlargement auricular fibrillation or congestive heart failure is an indication for early operation Only by such a radical measure can one hope to avert further cardiac damage and to restore normal cardiac function The indication becomes all the more urgent when there is an organic heart lesion such as valvular disease or coronary artery disease complicating the functional circulatory disturbance caused by the hyperthyroidism Whereas the heart that is otherwise sound will carry the stress of Graves s disease fairly well for years before becoming insufficient the already damaged heart gives way Hyperthyroidism increases the work of the heart in much the same manner as does physical exertion Just as one would not allow a patient with a crippled heart to engage in frequent or continuous physical exercise so in hyperthyroidism one must relieve the heart of its additional work as quickly as possible Only operation will accomplish this expeditiously and thoroughly In skillful hands the operative mortality is not great Lahey reports a 3 6 per cent mortality in operations on 138 patients with serious cardiac complications of whom 110 had congestive heart failure Of 101 patients who were traced 95 were returned to full activity 19 had persistent auricular fibrillation and 6 were still disabled Other operators have had results equally as good

Preoperative preparation with compound tincture of iodine is carried out as in all cases of hyperthyroidism In the presence of auricular fibrillation or heart failure full doses of digitalis should be given and the fluid intake should be

limited These patients usually tolerate large doses of digitalis without the appearance of toxic symptoms Operation should be delayed until the maximum restoration of cardiac function has taken place It is inadvisable to give quinidine sulfate preoperatively in an endeavor to abolish auricular fibrillation It is difficult to restore normal sinus rhythm in the presence of active hyperthyroidism Moreover, even if this result has been achieved recurrence of auricular fibrillation during or after operation is the rule It is wiser to try to control the heart rate with digitalis In patients with auricular fibrillation and no cardiac enlargement or heart failure it is unnecessary to give digitalis because the auricular fibrillation causes them little circulatory embarrassment In the majority of patients with auricular fibrillation complicating hyperthyroidism there is a spontaneous restoration of normal sinus rhythm after subtotal thyroidectomy If auricular fibrillation persists for two or three weeks following the operation quinidine therapy should be started unless there is marked cardiac enlargement

Adenomatous Goiter

Adenomatous goiters that have existed for decades without symptoms are seen from time to time in patients over 50 years of age They may by pressure cause narrowing of the trachea Breathing becomes wheezing and even stridulous Inspiration and expiration are prolonged Bronchial infection commonly develops This process leads to increased blood pressure in the pulmonary artery and strain on the right ventricle Adenomatous goiters may undergo malignant change or they may give rise to symptoms of hyperthyroidism In view of the potential troubles that may be caused by these adenomatous goiters it is wisest to remove them before the

give rise to symptoms and while the operative risk is minimal If any of the aforementioned complications occur operation is no longer a matter of choice it becomes a necessity irrespective of the condition of the patient

MYXEDEMA

Spontaneous myxedema occurs chiefly after middle age but is not common It is characterized externally by gain in weight a pasty complexion with puffiness of the face thickening of the skin and loss of hair The thyroid gland usually is not palpable The patient is sluggish his mental reactions may be dulled he complains of being cold and does not tolerate exposure to inclement weather The pulse rate is slow In long standing cases there is cardiac enlargement and heart failure may develop The electrocardiogram then shows low voltage of the QRS and T waves Arteriosclerosis and hypertension are not uncommon accompaniments of myxedema

Diagnosis rests on the discovery of a basal metabolic rate between minus 35 and minus 40 The blood cholesterol content is characteristically elevated to between 300 and 400 mg per 100 cc Basal metabolic rates ranging between minus 15 and minus 25 do not justify the diagnosis of myxedema unless there are characteristic symptoms and high blood cholesterol figures Such lesser depressions of basal metabolism are commonly observed with undernutrition and in thin asthenic persons who complain of a great variety of vague symptoms They do not indicate a primary diminished thyroid activity The reduced metabolism is a reflection of the same constitutional disorder that gives rise to the patient s symptoms Thyroid medication gives such patients little relief

The symptoms of myxedema can be abolished by admin

istration of desiccated thyroid Dosage must be cautious and the patient should be kept under close observation during the early stages of therapy Coronary arteriosclerosis and myocardial damage occur so commonly *in myxedema that a too hasty* whipping up of the metabolism may overtax the heart and quickly induce heart failure frequent anginal attacks or graver coronary insufficiency It is well to start with 1 gr of desiccated thyroid *once a day* This should be continued for one or two weeks If there are no untoward symptoms the dose may be doubled for the next week or two In the course of the following weeks further increases in dosage up to a maximum of 5 gr a day are permissible The maintenance dose is the smallest dose that will maintain a normal metabolic rate and give relief from symptoms If cardiac symptoms arise during the course of medication with desiccated thyroid, the drug should be stopped until the symptoms subside It should be recommenced with half the previous dosage and the patient should be watched closely At times prolonged treatment with small doses of desiccated thyroid eventually relieves the myxedematous state and restores the metabolism to normal More often cardiac symptoms arise when the basal metabolic rate reaches a level of from minus 20 to minus 25 In such cases it may be impossible and inadvisable to attempt completely to abolish the myxedematous state Just enough desiccated thyroid should be given to relieve the patient of the gravest symptoms Only by such measures can serious cardiac complications be avoided

Carcinoma of the Thyroid

Carcinoma of the thyroid rarely develops in diffuse toxic goiters It is encountered in 4 to 7 per cent of nodular or adenomatous glands and is especially prone to develop in a

solitary adenoma Like other thyroid disorders it is more common in women 80 per cent of patients being female It occurs at all ages from childhood on but the average age is 50 years An enlarged thyroid or a mass in the gland antedates the development of carcinoma by seven years on the average The two common forms are adenocarcinoma in which the tumor growth takes the form of the thyroid follicles which may contain colloid even in distant metastases or of a papillary adenocarcinoma The growth may be locally invasive break through the capsule of the gland invade the veins and by pressure on the trachea and esophagus cause dyspnea and dysphagia There is local extension to the cervical lymph nodes Metastasis through the blood stream which may occur when the primary lesion is still minimal in size localizes most commonly in the lungs and in the bones

Diagnosis is difficult and 80 per cent of cancers of the thyroid are first recognized by pathological examination of a gland that has been removed for other reasons A recently growing struma that is very hard and that is fixed to the surrounding tissues and does not ascend in the neck when the patient swallows should suggest malignancy The basal metabolic rate is usually normal Hyperthyroidism is not seen with malignant tumors of the thyroid gland Hypothyroidism in a case suspected of malignancy suggests that the lesion is due rather to chronic thyroiditis so called Riedel s struma

Once the diagnosis has been made operative removal is indicated even if a few metastases are demonstrable in the lungs or bones Operation should be followed by radiotherapy to the neck and to the metastases If operation is impossible radiotherapy should be carried out It is effective chiefly in the case of papillary tumors

Five year survivals are reported in 80 per cent of cases in which the diagnosis was first made by pathological study of

the gland in 40 per cent of those first diagnosed at operation and in 20 per cent of those diagnosed before operation These figures indicate the advisability of removing all nodular goiters without too much delay

Chapter Eighteen

DISORDERS OF THE BLOOD

THERE are no distinctive changes in the blood picture that come with aging. Persons over the age of 60 have somewhat lower values for hemoglobin and red blood cells than do those of younger ages. As is the case throughout life, the figures for women are lower than those for men. There is no characteristic alteration of the number and relative proportions of the white blood cells with advancing years. The total blood volume and plasma volume tend to diminish with advancing age and more so in men than in women.[1]

SECONDARY ANEMIA

Secondary anemia is due to iron deficiency in the body. This may result from massive or slow insidious loss of blood or from deficient ingestion or absorption of iron. Old people often exhibit idiosyncrasies of diet and may subsist largely on starchy foods and milk which contain very little iron. Lack of teeth or digestive disturbances that interfere with digestion or absorption of food may contribute to limitation of food intake. In time an iron deficiency results manifested by a secondary anemia. It is a common accompaniment of many

[1] Gibson, J. G., and Evans, W. A., Jr.: Clinical Studies of Blood Volume," J. Clin. Investigation 16:317, 1937.

chronic diseases Massive hemorrhage in older persons results most often from nosebleed in the presence of essential hypertension or from hemorrhage from a peptic ulcer Slow repeated or persistent hemorrhage is associated most commonly with bleeding hemorrhoids The anemia observed in patients with diaphragmatic hernia is caused by weeping of blood from the congested imprisoned gastric mucosa Gastric achlorhydria which is so common in the aged may contribute to the development of anemia by making more difficult the absorption of iron

In every case of secondary anemia the physician should first try to ascertain its cause and in particular rule out the presence of a neoplasm especially of the gastro intestinal tract and chronic nephritis with kidney insufficiency Estimation of the sedimentation rate of the red blood cells is a useful aid in ruling out malignancy The symptoms of secondary anemia depend on its degree In the milder cases the patient complains of weakness and because so commonly the cause is dietary he may have other symptoms of dietary insufficiencies If the hemoglobin drops below 60 per cent symptoms of dyspnea palpitation ready fatigue and possibly edema appear If there is an accompanying heart ailment with reduction of cardiac reserve, these signs become more prominent

The diagnosis rests on examination of the blood which reveals lowering of both hemoglobin and red cells with a low color index The red cells are small or of normal size The color of the skin of older patients is very deceptive and often a patient whose blood count is normal appears to be anemic Treatment involves control of any bleeding that may exist the provision of an adequate well balanced diet and the administration of iron This is best given in the form of ferrous sulfate or carbonate 5 gr three times a day

Ingestion of iron often induces constipation so that it may be necessary to give cathartics to keep the bowels open Liver extract is of no benefit in secondary anemia If the patient responds poorly to iron one or more transfusions may be needed

Hyperchromic (Pernicious) Anemia

Pernicious anemia is encountered chiefly between the ages of 40 and 70 About 60 per cent of cases occur after age 50 and 30 per cent after age 60 The maximum number of cases are between the ages of 50 and 60 Since pernicious anemia is caused by the absence of the intrinsic factor secreted by the stomach and since the loss of such a secretion just as the loss of hydrochloric acid may be expected to become more frequent with the years the age incidence is quite understandable When one allows for the lesser number of persons living at the higher age groups it is evident that the actual age specific incidence of pernicious anemia increases with the years

The symptomatology of pernicious anemia in the elderly does not differ from the usual picture described in the text books of medicine and it need not be elaborated in detail in this volume Characteristic are the hyperchromic macrocytic anemia with a high color index and accompanying leukopenia the elevated icterus index the absence of free hydrochloric acid in the stomach even after the injection of histamine the sore tongue with atrophied mucous membrane numbness and tingling of the extremities with signs of combined sclerosis of the spinal cord Loss of vibratory sense when tested with the tuning fork is the earliest neurological sign

Certain special problems arise with the diagnosis of per

nicious anemia in older persons The clinical picture may simulate cancer of the stomach As a rule the blood picture showing a macrocytic instead of a microcytic anemia leads to the correct diagnosis Patients with cancer of the stomach and marked anemia usually have lost much weight, an ab dominal mass may be palpable and there is blood in the stool The icterus index is not elevated The sedimentation rate of the red blood cells is of no aid in diagnosis I have seen a number of patients with pernicious anemia in whom the sedimentation rate was very rapid, and became normal when a remission was induced In every case of unexplained ane mia roentgen examination of the stomach should be under taken The occurrence of pernicious anemia and carcinoma of the stomach in the same patient is so frequent as to sug gest some basic relationship between the two diseases Au topsy studies show an incidence of 12 3 per cent of gastric cancer in patients with pernicious anemia Rigler and his associates in routine roentgen studies of 211 patients with pernicious anemia discovered 8 per cent with carcinomas and 7 per cent with benign polyps of the stomach Such polyps are often precursors of carcinoma The coincidence is so great that it would seem wise to subject patients with pernicious anemia to annual roentgen studies of their stomachs and to be on the watch for digestive disturbances that may signalize the development of a gastric neoplasm Cirrhosis of the liver may give rise to a hyperchromic macrocytic anemia that may be confused with pernicious anemia In these cases the cirrhosis is apt to be far advanced The history of the case, marked splenomegaly possibly ascites and the discovery of esophageal varices serve to differentiate the two conditions

Older patients commonly have coronary arterial disease,

Rigler L. C *et al* "Pernicious Anemia and the Early Diagnosis of Tumors of the Stomach J A M A 128 426 June 9 1945

and the impaired heart muscle does not stand up under the severe prolonged anemia Consequently angina pectoris may be a leading symptom With further myocardial damage congestive heart failure may supervene This picture was very common in the days before liver therapy was intro duced but is rare today The cardiac symptoms yield when the anemia is corrected

Treatment –This centers on giving enough liver extract to restore the blood count to normal and to maintain it there During the anemic stage it is best to give the liver extract intramuscularly at first 15 U S P units every two or three days When the hemoglobin and red blood cell count ap proach normal the intervals between injections can be lengthened to a week The maintenance dose varies with different patients 15 units every one two or three weeks is usually required If preferred oral preparations can be given daily instead In the presence of neurological symptoms treatment should be particularly intensive and there must be no relaxation when a remission has set in

Polycythemia Vera

True polycythemia occurs chiefly after age 50 Its cause is unknown It is characterized by a great increase in the hemoglobin in the blood and in the number of red cells The hemoglobin figures may reach 125 to 150 per cent and the red cells may number from 7 000 000 to 10 000 000 The blood volume is increased This serves to distinguish it from secondary polycythemia in which the volume of blood is unaltered The number of white blood cells too is elevated to between 15 000 and 20 000 cells and there is a relative in crease in the polymorphonuclear leukocytes

The disease comes on insidiously and the patient complains

chiefly of cerebral symptoms—headache or fullness of the head, vertigo, lassitude and irritability. He appears plethoric and of a dusky red color, particularly in the face. As a rule the spleen and liver are enlarged. Hemorrhages often occur. Thus there may be epistaxis, menorrhagia or even massive intestinal bleeding. I have seen a patient in whom the bleeding suggested a peptic ulcer. The roentgen picture of the chest reveals increased vascular markings of the lungs and at times curious discrete sharply outlined circular shadows that may represent thrombosed pulmonary veins. The course of the disease runs from 5 to 10 years. It is characterized by a great tendency to venous and arterial thromboses. Thrombosis may occur in any vein or artery. The most common sites are in the cerebral and coronary arteries and the arteries of the legs. Coronary thrombosis and cerebral vascular accidents are the usual causes of disability and death. At times after many years the blood picture changes to that of aplastic anemia or of leukemia and the patient dies from anemia and exhaustion of his bone marrow.

The best treatment is repeated phlebotomy performed with sufficient frequency to maintain the blood count at approximately normal figures. Acetylphenylhydrazine, a hemolytic poison, reduces the red blood cell count but is little used today because of the danger of excess hemolysis. Radiotherapy to the long bones and spleen is often beneficial. The diet should be poor in iron.

Secondary polycythemia is encountered most often with advanced pulmonary emphysema. In this condition, too, phlebotomy is helpful.

LEUKEMIA

There is some variance in the figures of the frequency of the leukemias at different ages. It is usually held that the

acute leukemias as well as chronic myelogenous leukemia are infrequent in older individuals All authors agree that chronic lymphatic leukemia occurs chiefly after age 50 In a series of 143 cases[3] however one half of the subjects with both the acute and chronic myelogenous leukemias were over 50 and 40 per cent of those with acute lymphatic leukemia and 88 per cent of those with chronic lymphatic leukemia were over 50 Monocytic leukemia too is most common after the fifth decade All forms of leukemia but particularly the chronic lymphatic form are more common in males than in females

Leukemias in elderly persons do not differ from those in the young Anemia loss of weight enlargement of the lymph nodes liver and spleen are the characteristic features of the chronic forms of the disorder The basal metabolic rate is elevated The prognosis for all leukemias is poor Patients with chronic forms particularly lymphatic leukemia may survive many years although the average duration is from three to four years Treatment is unsatisfactory Fowler s solution given to the point of tolerance seems to benefit some patients with chronic myelogenous leukemia Isaacs recommends the employment of radiotherapy only when there is progressive anemia or when there are marked nervousness weight loss tachycardia sweating and sleeplessness It may be useful in reducing the size of a very large and heavy spleen Repeated transfusions are of benefit when there is anemia

Acquired Hemolytic Jaundice

Hemolytic jaundice may have its onset after the age of

[3] Kirshbaum J D and Preus F S Leukemia Arch Int Med 71 777 June 1943

50 it has been observed in the eighth decade[4] In such cases there is no family history or previous indication of the dis order *There is rapid development of hemolytic anemia* with weakness palpitation dyspnea pallor and jaundice The spleen and liver are enlarged In some cases there is increased fragility of the red blood cells in hypotonic salt solutions together with spherocytosis Splenectomy may lead to im *provement and may indeed be life saving* It is particularly effective in patients with increased erythrocyte fragility

[4] James D F and Evans L R Splenectomy for Acquired Hemolytic Jaundice in the Aged" New England J Med 233 143 Aug 2 1945

Chapter Nineteen

DISEASES OF THE EYES

THE EYES manifest many signs of aging The orbital fat becomes absorbed so that the eye sinks deep into its socket The eyelids lose their tonicity so that eventually the upper lid may droop and the lower lid may be everted The sclera takes on a yellowish color as a result of fatty changes The color of the iris fades and the pupil becomes small and less mobile The arcus senilis the circular lipoid infiltration at the circumference of the cornea may occur among younger persons but becomes increasingly frequent with advancing years Its incidence at different ages is shown in Table 7 [1]

TABLE 7 Incidence of Arcus Senilis

Age	Arcus Senilis Per Cent	
	Male	Female
30-39	5 5	0
40-49	10 0	1 0
50-59	2[illegible] 0	19 0
60-69	[illegible] 0	30 0
70-79	73 0	1[illegible] 0

With age comes loss of visual acuity This is shown in all of the physiological functions of the eye the visual fields become smaller and the power of accommodation is lessened Old people require greater intensity of light for close vision

[1] Boas E P Arcus Senilis and Arteriosclerosis" J Mt Sinai Hosp 1° 79 May June 1945

and thus should have stronger illumination for reading or other similar use of their eyes They see less well in the dark The steady decline in the capacity for dark adaptation that comes with aging is due to the progressive decrease in the size of the pupil[2] There is a lessened ability to match colors after age 65[3] The lens grows less and less elastic and calls for ever greater accommodative efforts on the part of the patient When such accommodation can no longer be made the condition of presbyopia develops the patient cannot focus on nearby objects cannot read and needs glasses for near vision He has no difficulty with far vision Bernstein has demonstrated a definite correlation between the age of onset of presbyopia and longevity On the average those who develop presbyopia early die at younger ages than those in whom presbyopia develops late in life and these early presbyopics tend to die of arteriosclerotic heart disease[4] The so called second sight a condition in which a person who has required glasses for near vision can do without them in late life is due to an increasing shallowness of the anterior chamber of the eye and increased refractive power of the nucleus of the lens

Blepharitis and conjunctivitis are common in older persons The palpebral conjunctiva becomes congested and red Calcareous concretions consisting of dead epithelial cells and hardened mucus may form in the serous glands of the conjunctiva

Some of these senile changes in the eye require treatment

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[2] Robertson G W and Yudkin J "Effect of Age upon Dark Adaptation" J Physiol 103 1 June 1944

[3] Smith H C "Age Differences in Color Discrimination" J Gen Psychol 29 191 1943

[4] Bernstein F "Law of Physiologic Aging as Derived from Long Range Data on Refraction of the Human Eye" Arch Ophth 34 378 Nov Dec 1945

When the upper lid droops enough to interfere with vision and when eversion of the lower lid leads to tearing and conjunctivitis these deformities can be corrected by simple plastic operations Calcareous concretions of the conjunctiva should be removed Presbyopia calls for the prescription of glasses for near vision The strength of the glasses should be determined not alone by the degree of impairment of accommodative power but also by the chief occupation of the patient Thus a person who reads and writes a good deal should have an adjustment that will allow for nearer vision than a musician an artist or a typist At times it is well to provide an intermediate pair of glasses that afford easier vision at card playing or at some other activity that calls for less close application

Disease conditions that lead to failing vision of the aging person are primarily vascular changes of the fundus central macular senile degeneration cataract and simple noninflammatory glaucoma

Vascular changes of the fundus characteristic of the aged are due to simple retinal arteriosclerosis and are unrelated to arterial hypertension The arteries of the eyegrounds become tortuous and there may be degenerative lesions in the retina Hemorrhages occur but are infrequent The more striking picture of narrowed arteries edema exudates hemorrhages and scars are associated with arterial hypertension and do not differ from similar vascular lesions at younger ages Senile degeneration of the macula is probably also of vascular origin The condition is bilateral Central vision becomes impaired and when the process is complete there is a central blind spot Treatment is of no avail

Cataract is the chief cause of blindness after the age of 65 Although cataract formation is closely related to aging of the lens hereditary factors play a role in some cases Cataracts

may appear in siblings when they reach the same age Nuclear changes with some haziness of the lens and minor opacities may be found in over 90 per cent of persons past the age of 65 Many of these small opacities do not progress to full cataract formation The later in life that opacities of the lens appear the less likely are they to cause loss of vision A cataract that begins after the age of 60 is far less apt to mature than one that begins one or two decades earlier If cataract occurs in only one eye the patient may be unaware of it for the good eye takes on the task of both But gradually there develops some interference with vision When an early cataract is centrally placed the patient s near vision may improve for a time because of the increased refractive power of the denser lens But distant vision is impaired and bright objects may appear blurred or double With a central opacity, the patient sees better in dull light which allows the pupil to dilate permitting light to pass through the peripheral parts of the lens In the case of peripheral opacities vision is better in a bright light for the central part of the lens is clear and the contracted pupil shuts out the distorted images that arise by light passing through the peripheral opacities

The thought of cataract with possible resultant blindness strikes terror into the hearts of most persons Therefore when a cataract is discovered the physician should take great pains to explain the full situation to the patient He must make clear that most cataracts mature very slowly that for years the patient may preserve satisfactory vision and that if blindness finally comes on it can usually be relieved by operation The patient s vision can be aided in various ways In the case of central cataract if there is no glaucoma the instillation in each eye every morning of a drop of 1 per cent homatropin and 5 per cent ephedrine solution will dilate the pupil sufficiently to improve vision Reading is facilitated by the

use of a rubber sheet about half the size of the page of a book This contains a slit 4 in long and ¼ in wide It is placed on the page of reading matter so that one line of type shows through the slit This device makes reading easier because it lessens the amount of light reflected from the white page and so lessens pupillary contraction and eliminates the blurred images of peripheral vision When the cataract finally becomes mature it should be extracted Before operation the surgeon should make sure that retinal function is still intact The pupil should react to light and the patient should perceive light

The characteristic glaucoma of the aged is simple non inflammatory glaucoma It has a familial occurrence gives rise to little pain pursues an insidious course and may result in serious permanent impairment of vision before it is recognized The patient complains of occasional slight blurring of vision commonly more marked in one eye When in a dim light or when emotionally upset he may experience some pain in the eyes after visiting a motion picture performance his eyes may feel strained or uncomfortable There is some impairment of vision and the patient has his glasses changed frequently without relief These symptoms progress very slowly Only when the condition is far advanced does the patient notice halos or rainbow effects about lights Examination may reveal few physical signs The intra ocular tension is not continuously or greatly elevated it is apt to be higher in the late afternoon or when the patient is under strain The hardness of the eyeballs should be gaged by palpation with the fingers and careful measurements with the tonometer should be made The pupils may be unequal and may react sluggishly to light Central vision for reading is at first preserved but careful examination reveals subnormal vision in one or both eyes with irregular contraction of the peripheral

field of vision Cupping of the optic disk observed through the ophthalmoscope is a late phenomenon All too often the diagnosis is overlooked until it is too late and complete blindness results This error is especially common when cataract and glaucoma occur simultaneously The failing vision is ascribed to the cataract and the glaucoma is allowed to progress Finally when the cataract is ripe operation does not restore the vision that has been completely destroyed by the glaucoma Aging persons should have their eyes checked yearly and every examination must include measurement of the pressure of the eyeball The treatment of glaucoma should be in the hands of a skilled ophthalmologist He will determine whether conservative treatment with miotics or operation is indicated

Acute glaucoma occurs chiefly between the ages of 45 and 65 It has no distinctive characteristics when it appears in aging persons

Chapter Twenty

DISEASES OF THE SKIN

THE SKIN of the aging person loses its elasticity and becomes wrinkled. The epidermis, especially the malpighian layer, becomes thin, the basal layer is pigmented, the papillae are flattened, and the elastic fibers and the subcutaneous fat disappear. Gradual atrophy of the sweat and sebaceous glands leads to dryness and roughness of texture. Eventually, when the skin grows very thin, it becomes smooth and glossy. Seborrheic keratoses appear, particularly on the trunk and face. They are slightly elevated, greasy, flat, yellowish brown to black plaques and may be numerous. They have no clinical significance and can be ignored. Excessive bathing and the use of strong soaps remove the scanty fat supply of the aging skin, increase its dryness, and lessen its resistance to external irritants. An emollient such as cocoa butter or an ointment made of equal parts of lanolin and petrolatum often gives relief when the skin is very dry.

Graying of the hair and baldness are accepted by the laity as evidences of aging. Yet there is great variability in the age at which these phenomena appear. Hereditary influences play a strong role. The average age at which gray hairs first appear is 34.2 ± 8.6 years for white men and 43.9 ± 10.3 years for Negro men. In general, however, light hair becomes gray later in life than does dark hair. While the hair of the

scalp thins, the hair of the nose ears and eyebrows increases in amount and becomes thick and bristle like In women hair appears on the upper lip and on the chin

Senile keratoses are small elevated horny growths covered with scales that appear on the exposed parts of the skin These keratoses may undergo carcinomatous metaplasia—particularly if they occur at a site that is constantly irritated by clothing Such growths should be removed preferably by radiation therapy They tend to recur and often new ones form

Leukoplakia of the mouth occurs as white thickened patches on the mucous membrane of the cheeks or of the tongue It may result from syphilis from excessive smoking or chewing of tobacco or from imperfect teeth Leukoplakia commonly forms the nidus for the development of cancer Pipe smokers may develop cancer at the tip of the tongue Those who chew tobacco are apt to develop a lesion on the inner aspect of the cheek where the quid is held Ragged stumps of teeth or poorly aligned bites may produce sufficient irritation of the mucous membrane to induce leukoplakia or cancer In the presence of leukoplakia smoking must be stopped completely The teeth should be put in good condition In old people the physician should pay strict attention to the hygiene of the mouth for neglect on the part of the patient is common

Basal cell epithelioma or rodent ulcer is not confined to the aged The average age at onset is given as 45 years It is a slow growing lesion that begins most often on the face above the level of the nostrils as a warty growth that ulcerates It remains superficial and for a long time does not penetrate deeper than the superficial fascia Gradually the growth extends at the periphery and the center ulcerates and is filled with granulation tissue The edges of the ulcer are raised and

nodular Ultimately it may invade and erode deeper tissues and neglected cases are seen in which the eye ear or nose has been destroyed or the maxillary sinus invaded The lymph nodes are never involved Early diagnosis is essential and every suspicious lesion must be subjected to biopsy With modern methods of radiotherapy fully 98 per cent of these growths can be cured by the use of appropriate technics

Squamous cell epithelioma has its highest incidence in the seventh decade and usually arises from senile keratoses It is a true malignant neoplasm which grows rapidly and metastasizes The base of the lesion is infiltrated ulceration and bleeding are the rule Every such lesion of the skin should be regarded with suspicion, and a section removed for biopsy whenever there is the slightest doubt Early epitheliomas can usually be cured by radium or roentgen therapy but treatment must be individualized In some cases excision or electrocautery and in others curetting and the application of caustics followed by radiotherapy are the methods of choice

Senile pruritus is one of the most distressing and stubborn conditions encountered in the aged It should not be assumed that itching of the skin in every elderly person is due to senile changes It is always essential to rule out such causes as pediculosis scabies eczema diabetes Hodgkin s disease and azotemia When no definite cause can be determined when the skin is dry thin and atrophic when the condition is aggravated by cold and by frequent bathing one may assume that one is dealing with true senile pruritus Treatment in the past has consisted largely of the application of soothing emollients or calamine lotion possibly with the addition of some phenol Recent observations indicate that treatment with the *sex hormones* may give complete relief from senile pruritus Women are given injections of 1 mg estradiol dipropionate and men 25 mg of testosterone propionate about

every five days until the symptoms are controlled If the injections are stopped the symptoms will return in a few weeks so that treatment must be continued indefinitely, but the injections can be spaced at longer intervals Some patients require higher dosage some less In each case the optimum dose must be determined by actual clinical trial

Varicose Veins and Ulcers of the Legs

Varicose veins and their sequelae may first appear in youth They occur most frequently in early middle life If untreated they cause increasing disability and in older patients they are often responsible for chronic eczema infection and ulceration of the legs Varicose dilatation of the leg veins may be a primary condition or it may represent a collateral circulation secondary to phlebitis and occlusion of the deep veins of the leg The cause of the development of primary varicosities is not understood There is a marked hereditary factor, for a familial incidence of varicose veins is found in over one half of all cases Absence or incompetence of the valves in the perforating veins of the saphenous systems probably represents the underlying defect Occupations that compel standing for many hours pregnancy and abdominal tumors may contribute to the venous stasis and accelerate the process

In well marked cases the internal saphenous veins stand out as thick cords extending down the thighs In the popliteal space and in the leg are large bunches of tortuous dilated veins In milder cases only small superficial veins are dilated as spider bursts or only a few of the veins of the legs are dilated When the varicosities are secondary to occlusion of the deep veins anastomotic channels to dilated veins on the abdomen and trunk are usually visible

The patient complains of heaviness ... In time edema of the legs appears. The ... and subcutaneous tissues suffers as a re... impairment of blood flow and the skin ... and indurated. As a result of repeated ... rhages and diapedesis of red blood cells ... tion of the skin develops. Often there is prur... g by the patient further traumatizes the sk... the skin is common and is often made worse b... fection of the feet. Eczematous eruptions comm... Finally the tissues break down and ulcers of the ... These ulcers are very persistent and heal with dif...

Treatment.—When there is much eczema and ... this must be brought under control before the vein... selves are treated. The patient is put to bed and the ... vated. If there is extensive weeping eczema wet dres... applied. Five per cent alcoholic solution of gentian vi... applied to the ulcers and to areas infected by fungus. A... infection subsides and the skin becomes dry the leg ... posed to the air. Ultraviolet radiation may be helpful.

When the leg is in optimum condition the veins ... obliterated. When the phlebectasis is not extensive ... ticularly when the internal saphenous vein is litt... injection of the veins with a sclerosing solution ... factory results. This is a surgical procedure ... rhuate in a 5 or 10 per cent solution is favored ... tors. Occasionally allergic reactions to this ... countered. Other operators use quinine ... urethane. If there are marked incompetence ... ous femoral valve and dilatation of the ... vein injection alone will not be successful ... tion of this vein at the saphenofemoral junc... ried out after first establishing the compe...

veins The superficial veins are then injected Treatment carefully carried out is successful in the majority of cases There may be recurrences due to recanalization of the induced thrombi or to marked incompetence of some of the communicating veins between the deep and superficial venous systems At times ulcers do not heal and have to be excised the exposed area being covered by skin grafts Varicose veins that arise as compensatory channels as a result of thrombosis of the deep veins of the leg should not be obliterated If they cause distress the patient should wear bandages or elastic stockings

Chapter Twenty One

DISEASES OF THE NERVOUS SYSTEM

IN ADVANCED age the brain undergoes involution There has been much controversy just as there has been in the field of arteriosclerosis as to whether these changes represent the aging process as such or whether they are the result of the innumerable vascular and toxic insults to which the brain has been subject during the long years of life [1] There is great variability in the occurrence of senile changes in the brain Anatomic study of the brains of some persons who have died in the ninth decade has revealed remarkably few changes these were individuals who had retained their full mental faculties up to their death In general the aged brain is shrunken and firm its surface is wrinkled its fissures wide its ventricles dilated The process is especially marked in the frontal lobes The gray matter of the cortex may have a worm eaten appearance Many of the nerve cells are atrophied and there is an increase of intracellular pigment The nerve fibers are diminished in numbers There is an increase in the corpora amylacea There may be many small foci of softening The so called senile plaques dense circular areas with an amorphous center especially studied by Alzheimer and by Simchowicz are interpreted by many as characteristic

[1] Tilney F Aging of the Human Brain Bull New York Acad Med 4 1125 1928

of senile involution of the brain In normal persons they do not occur before the age of 75 or 80 and then are few in number After the ninetieth year they are always found In persons who die at earlier ages with senile dementia these plaques are present in great numbers and they are particularly numerous in precocious senile dementia (Alzheimer's disease)

Old age brings with it a general dulling of the senses Vision becomes dim, hearing less acute the senses of taste and smell less discerning The taste buds in the circumvallate papillae become fewer with the years especially after age 75[2] The number of fibers in the olfactory nerves decreases progressively throughout life[3] Responses to pain and to touch are less marked With every decade there is a slight diminution in the vibratory sensibility of the lower extremities This becomes marked after age 50 and in many older persons vibratory sensibility of the legs is absent This change is believed to be due to vascular lesions in the posterior columns of the spinal cord[4] Motor disturbances reflect lesions of the extrapyramidal tracts The body tends to assume attitudes of flexion[5] The head and neck are bent forward and the elbows wrists hips and knees assume the position of semiflexion Rigidity of the limbs may develop There is a diminution of muscular movement what may be called a poverty and slowness of movement with a tendency to prolonged immobility The senile gait with the legs apart giving a widened base to the body the body and legs some

[2] Arey L B *et al* "The Numerical and Topographical Relations of Taste Buds to Human Circumvallate Papillae throughout the Life Span" *Anat Rec* 64 9 1935

[3] Smith C G "Age Incidence of Atrophy of Olfactory Nerves in Man J Comp Neurol 77 589 1942

[4] Pearson G H J Effect of Age on Vibratory Sensibility Arch Neurol & Psychiat 20 482 1928

[5] Critchley M Neurology of Old Age" Lancet 1 1119 May 31 1931

what flexed and the steps shortened is the direct result of these extrapyramidal changes When these changes are sufficiently advanced they may lead to a propulsive gait When well developed all of these phenomena give the typical picture of parkinsonism

Tremors are common They are rapid and fine and involve the head the lower jaw the hands and the forearms They are exaggerated by emotion and fatigue and abolished during sleep Simple senile tremor is not associated with rigidity The reflexes may be diminished and the knee and ankle jerks are often absent

The most common neurological disorders of the aged are caused by arteriosclerosis of the cerebral arteries These have been discussed under the section on arteriosclerosis They may manifest themselves as frank hemiplegias or give the clinical picture of multiple cerebral vascular insults or of cerebral softening Cerebral softening due to gradual atherosclerotic and thrombotic occlusions of cerebral arteries is the typical lesion of the aged There may be prodromata such as headache vertigo or somnolence followed in a few days by paralysis of one side of the body or of one limb There may be mental confusion or impairment of memory Characteristically there is a slow progression of symptoms over a period of years There are more and more loss of motor function and progressive destruction of the intellectual faculties Eventually loss of sphincter control develops and the classic picture of arteriosclerotic dementia sets in Multiple bilateral cerebral lesions may lead to the syndrome of pseudobulbar palsy The facies are expressionless but the patient has paroxysms of laughing and crying without cause The mouth is held partly open and there is drooling of saliva The voice is nasal without timbre and without expression The motor signs are those of multiple lesions of the pyramidal tract

Paralysis Agitans or Parkinson's Disease

Paralysis agitans is a disease of later life characterized by tremor and muscular rigidity. It should be distinguished from the Parkinson syndrome that follows epidemic encephalitis and occurs in young persons. The lesions responsible for this disorder are widespread: in the cortex, the corticothalamic connections and in the basal ganglions. The substantia nigra is most constantly involved, and the pyramidal system is spared.[6] Some cases are the end result of an unrecognized encephalitis, others of arteriosclerotic softening and in still others the cause cannot be determined.

The average age at onset is between 50 and 55. Progress of the disease is slow. It may last 10 to 30 years and does not appreciably shorten the life of its victim. The disease begins insidiously, often with rheumatoid pains and weakness of the extremities. Tremor is the first distinguishing sign. As a rule it first becomes manifest in the small muscles of the hands and involves the thumb and index finger, which undergo from four to seven flexions a second, giving rise to the so-called pill-rolling movement. Gradually, in the course of two to four years, the affected area extends to involve the wrist and the forearm. The muscles of the calf and the toes may also give evidence of the disturbance. Finally the muscles of the face become affected; there is tremor of the tongue and of the lips, and there may be a tremor of the head. The facial muscles themselves are usually immobile and rigid and give rise to the expressionless masklike facies. The tremor is present at rest, becomes less on voluntary motion and ceases during sleep. At times the symptoms are restricted to one half of the body.

[6] Benda, C. E., and Cobb, S.: On the Pathogenesis of Paralysis Agitans, Medicine 21: 95, May 1942.

Muscular rigidity is an essential part of the clinical picture This tends to keep the trunk and extremities in the position of flexion The head is flexed on the trunk the trunk is bent forward and the arms and legs even in walking are held in the position of semiflexion The muscular rigidity offers resistance to passive stretching of the muscles and it is difficult to straighten the patient s limbs There is great delay in initiating movement and a considerable latent period elapses between the giving of an order and the execution of a movement on the part of the patient Movement is slow deliberate and difficult For the same reason speech is slow deliberate low and monotonous Walking is seriously affected The patient gets up with difficulty and starts off with a slow shuffling gait Then bent forward he takes faster and faster small steps exhibiting the typical propulsive gait In extreme cases he will fall forward if his progress is not arrested While walking the body is rigid and there are no automatic and associated movements such as swinging of the arms The body moves as though made of one piece—like a piece of machinery to use Parkinson s simile As a result of the muscular rigidity and the difficulty in executing movements the patient tires very easily

Throughout the course of the disease the mind remains clear, even though the lifeless facies the slow reactivity and the halting speech often suggest mental impairment For years there may be only slight tremor of a few fingers but gradually and inevitably more and more muscle groups become involved and greater and greater rigidity sets in Eventually the patient becomes completely helpless as a result of the generalized rigidity He can no longer walk cannot feed himself or execute the simplest movements to help himself This state may last for five or six years before death finally brings release

Treatment —General treatment is concerned with maintaining nutrition and assisting the patient to keep up and about and active Massage warm baths and passive movements of the extremities are helpful For years belladonna and scopolamine have been used with varying results More recently exceptional virtues have been attributed to Bulgarian belladonna Further studies have revealed that its efficacy lies not in the root itself but in the method of extraction A vinous extract of the American roots is as efficacious as the extract of the Bulgarian variety Apparently extraction with white wine gives a different preparation than extraction with alcohol Such a preparation is available under the name of Vinobel Each tablet contains 0 4 mg of the total alkaloids Dosage is commenced with 1 tablet a day and the amount is increased by 1 tablet daily until the optimum effects are obtained or until toxic symptoms appear The average dose required for each patient differs on the average 7 to 10 tablets a day are needed Some patients do well on 3 tablets others may require 20 or more Toxic symptoms are those of atropine poisoning mydriasis loss of accommodation dryness of the mouth a hot flushed skin and tachycardia Symptomatic improvement of parkinsonism is manifested chiefly by lessening of the rigidity and salivation and increase in strength and sense of well being The tremor is little affected The postencephalitic type of parkinsonism responds especially well to this treatment and some authors claim maximum improvement in over half the cases The same results can be obtained by the use of atropine sulfate The patient is given a ½ per cent solution of which each drop contains 1/200 gr of atropine The initial dosage of 1 drop three times

[7] Fabing H D and Zeligs M A "Treatment of the Postencephalitic Parkinsonian Syndrome with Desiccated White Wine Extract of U S P Belladonna Root" J A M A 117 332 Aug 2 1941

a day is gradually increased to between 5 and 10 drops three times a day Older persons with paralysis agitans due to degenerative disease benefit less often and may not tolerate the necessary large doses of the drug They should however be given a trial because some are helped In the presence of glaucoma belladonna products should not be used and when there is accompanying cardiovascular disease they should be employed with care

Highly satisfactory results have been reported from the administration of vitamin B_6 (pyroxidine hydrochloride)[8] The patients receive from 50 to 100 mg of pyroxidine hydrochloride intravenously daily for from two to four weeks The maintenance dose must be adjusted to the needs of the patient Astonishing results have been reported with marked reduction in rigidity and tremor and great gain in strength Even long standing advanced cases have been improved The arteriosclerotic type of the disease responds better than the postencephalitic form

The recently isolated active principle of curare tubocurarine is being employed to relieve muscle spasms of all sorts Tubocurarine depresses the myoneural junction Dosage can be adjusted to block abnormal impulses without loss of voluntary power of the muscle Given to patients with parkinsonism it relieves rigidity but not the tremor[8a] Patients get great relief from such relaxation often lose the pain from muscle tension and are able to sleep A 3 per cent solution of tubocurarine is prepared in 4 8 per cent wax in peanut oil This preparation can be sterilized The average dose is 1 cc subcutaneously or intramuscularly The action

[8] Baker A B Treatment of Paralysis Agitans with Vitamin B (Pyroxidine Hydrochloride) J A M A 116 2484 May 31 1941

[8a] Schlesinger E B Curare A Review of Its Therapeutic Effects and Their Physiological Basis Am J Med 1 518 1946

commences within a few hours and may last for several days Subsequent doses are given when the effect of the previous dose wears off No toxic effects are observed when the drug is given in this manner

Senile Chorea

Senile chorea is a so called degenerative disease occurring after the age of 50 characterized by gradually increasing general choreiform movements The patient usually has an unstable irritable personality and often develops paranoid trends At autopsy, senile plaques have been found in the putamen and caudate nucleus It has been suggested that this is a form of Huntington's chorea that appears late in life[9]

Meniere's Syndrome

Meniere's syndrome characterized by attacks of true vertigo, with nausea and vomiting and associated with tinnitus and progressive deafness, occurs at all ages chiefly in the fourth fifth and sixth decades of life One third of the patients are over 50 at the time of onset of the disease The condition warrants discussion because it is so frequently incorrectly diagnosed and in older persons is too readily attributed to a disturbance of the heart or arteries

The syndrome is caused apparently by pressure or chemical changes in the endolymph with secondary involvement of the sensory end organs in the semicircular canals and the cochlea[10] The nature of these changes remains obscure but

[9] Rothschild D "Senile Chorea and Its Relation to Huntington's Chorea" J Mt Sinai Hosp 5 517 1938

[10] Crowe S J "Meniere's Disease" Medicine 17 1 February 1938

Atkinson[11] suggests that in a small proportion of cases allergic reactions may be responsible and that in the others vaso spastic disorders in the internal ear may underly the disturb ance Others have suggested that disorders of water metab olism or of electrolyte balance particularly of sodium may be the determining factors All observers agree that the dis order bears no relationship to systemic disease to arterio sclerosis or hypertension or to otitis media It is not due to cerebral arteriosclerosis

The attack can occur at any time even during sleep In some cases increase in tinnitus or fullness of the head may warn of an impending seizure In the attack the patient is seized with intense vertigo all of the surrounding objects appear to revolve rapidly about him Nausea and vomiting follow The attack may last minutes hours or days In severe attacks the patient may be thrown to the floor by the violence of the vertigo and may even faint as a result of sudden drop in blood pressure Under such circumstances the incorrect diag nosis of coronary occlusion is often made At times the severe vasomotor disturbances may induce a coronary insufficiency of sufficient degree to cause cardiac infarction

The patient is usually compelled to lie immobile for move ments of the body particularly turning the head bring on renewed vertigo Physical examination during the attack and afterward is unrevealing The pulse rate and blood pressure are normal, and a careful neurological examination may de tect no abnormalities There is no middle ear disease Caloric tests may show normal diminished or absent vestibular func tion Audiometer tests reveal some impairment of hearing on the affected side The side that is involved can usually be recognized by noting the ear in which tinnitus is experienced

[11] Atkinson M "Observations on the Etiology and Treatment of Meniere s Syndrome" J A M A 116 1753 Apr 19 1941

Once the attack is over the patient feels quite well except that tinnitus usually persists The spacing of attacks is variable they may come very frequently or there may be remissions of months or years Deafness is slowly progressive

Treatment —Many forms of treatment have been suggested but all are difficult to evaluate because of the natural tendency to long remissions Some have advocated restriction of fluid and sodium intake Atkinson tests all patients with an intradermal test dose of 0 01 mg of histamine dihydrochloride If in response to this injection a large wheal with pseudopods forms the case is considered allergic attempts are made to eliminate possible allergens in the food or surroundings and desensitization with histamine is undertaken The majority of patients do not fall in this category These are treated with nicotinic acid approximately 25 mg intramuscularly daily at first then at longer intervals In the attack the slow intravenous administration of 1 9 mg of histamine acid phosphate in physiologic salt solution over a period of an hour and a half may induce a dramatic cessation of the seizure I have found aminophylline or theobromine sodium acetate with phenobarbital useful In patients who resist all treatment and in whom the attacks of vertigo are disabling section of the vestibular nerve cures the vertigo but leaves the tinnitus unaffected The operation may lessen the degree of deafness

Guillain Barre Syndrome

This is an infectious radiculoneuritis that occurs at all ages In the young recovery is the rule but in older persons the disease is apt to be more severe and the mortality approaches 40 per cent[1] The neurological disorder is usually

[12] Baker A B Guillain Barre s Disease in the Older Age Group" Geriatrics 1 132 Mar Apr 1946

preceded by an infection of the respiratory tract Then polyneuritis develops with severe radicular pain muscle tenderness and flaccid paralysis of the extremities Facial nerve palsy is common In older patients extension to the bulb with multiple cranial nerve palsies is frequent The disease may take a myelitic form with bladder paralysis and rectal incontinence There is little fever or leukocytosis The findings in the spinal fluid are characteristic there is an increase in the protein content without pleocytosis Treatment is symptomatic

Herpes Zoster

Herpes zoster is more frequent in the young than in the old but in older persons the postherpetic pain is apt to be exceptionally severe and persistent Otherwise its clinical course does not differ in the various age groups There is an apparent relationship between herpes zoster and varicella It is not uncommon for a grandparent to develop zoster after one of the grandchildren has had chickenpox I have also seen chickenpox develop in a child exposed to an older person who had herpes zoster Herpes zoster is caused by a virus infection of the posterior ganglia There is also a symptomatic form of zoster that develops when a posterior ganglion is invaded by a neoplasm or is the site of trauma or hemorrhage Treatment of persistent root pain following the eruption is difficult Often codeine and aspirin must be given for many weeks Injections of 0 5 cc of posterior pituitary extract are said to be helpful Roentgen therapy to the region of the affected ganglion often relieves the pain

Mental Disorders

Certain aspects of the mental changes that come with age and some problems of mental hygiene of the aged have been

discussed in Chapter 2 Physicians and laymen alike are too apt to attribute any and every mental disturbance in old people to organic regressive changes in the brain or to regard them as evidences of senile dementia As a consequence no treatment is attempted and mental deterioration progresses until an irreversible state is reached It has been estimated that fully one quarter of patients with a diagnosis of senile or arteriosclerotic dementia can make social recoveries if given proper treatment Psychoneuroses are common among the aged The aging brain with its impaired blood supply has not the metabolic reserve power to withstand toxemia nutritional lacks or severe circulatory disturbances and manifests its insufficiency by delirious reactions Such disturbances may be superimposed on true psychoses or dementias Thus it is vital to attempt an accurate diagnosis in every instance of mental disorder in the aged for as we shall see treatment often has gratifying results

PSYCHONEUROSES

Bleuler has said Senility often becomes a disease only as a result of the sudden cessation of the ordinary attractions of life The changing social status of the aged forces them to make so many adjustments to their environment that it is not astonishing that many of them develop psychoneuroses In some persons the neurosis repeats or continues the patterns of their younger years The mental disturbance may be traced to the patient s inability to adapt to new situations to the personal difficulties brought on by the declining years of life Adjustment to these impacts depends in part on the habitual reactions built up in one s younger years

Sooner or later every elderly person must face the fact that his body is aging There is a decrease in strength and in skills, the skin visibly becomes thin and wrinkled the hair

gray and scanty there may be impairment of sight and hearing of sexual power and the woman becomes aware of the loss of her good looks Some persons have a sudden realization of their failing bodily powers some specific incident—the inability to perform some act formerly carried out with ease failure to hold their own among their companions—drives home to them awareness of their waning powers Handicapping illnesses may have a similar effect Of equal or possibly of even greater importance is the impact of the cultural traditions of society Loss of gainful work with stoppage of income leads to dependence of the aging worker to loss of his own home with a readjustment of his mode of life often to enforced residence with his children as an unwanted guest The aging person learns that he has become useless that he is no longer an important member of society Abrupt retirement from ones life work which is becoming increasingly common in our industrial civilization involves a radical change in the habits and customs of living and in ones outlook on life There is a loss of incentive and of routines of living that have been built up over the years In many instances loss of home and of accustomed routine leaves the aging person with no privacy into which he can retreat

As a result of all of these attacks by a hostile environment on the essence of his living the old person either fights for self preservation and develops aggressions or finding the situation too difficult for his waning powers retreats into fantasy He acquires anxieties The mechanism of the neuroses in the aged does not differ from that in younger persons Anxiety is commonly transferred to the visceral functions of the body The aging person becomes absorbed in the natural operations of his digestive tract develops a too great interest in his bowel habits or acquires dietary idiosyncracies because

of digestive symptoms He may develop palpitation or other cardiovascular symptoms These complaints which may become hypochondriacal are often used to maintain domination over his children and may be tools to give the children a sense of guilt—they are aggressive tendencies Depression may develop or there may be excessive fatigue Other aging individuals may withdraw from life and evince little interest in their environment They may develop exaggerated routines of living which may become compulsions Lack of interest in what is going on about them in a world in which they no longer have a part contributes to their forgetfulness of recent events and they find refuge in reminiscence Small wonder that many are so lonely tired and hopeless

Many elderly men and women continue to have normal sex impulses but because of the social environment and the general view that old people should be beyond such desires they find normal gratification difficult they often resort to masturbation and this gives rise to a sense of guilt The thwarted sex impulse commonly gives rise to anxiety or to hypochondriacal symptoms of low back pain and dysuria

The steadily increasing numbers of the aged make it all the more important that society give some thought to their social problems to preserving some sphere of economic usefulness and self sufficiency to its growing numbers of industrial derelicts Only by social planning can the many real problems and difficulties of the aged be met and only by some such means can many older persons be prevented from developing psychoneuroses Treatment of the psychoneuroses must lean heavily on the social readjustment of the individual on finding ways of granting him the needed self expression the security the independence the self respect which he requires Both individuals and society should prepare years in advance for the age of retirement to find some

means of making such retirement gradual of preserving some self sufficiency to the aging member When an old person is suddenly thrown in the discard it is too late to teach him how to meet the onslaughts of life by rebuilding his character He needs some routine some grooves of usefulness to guide his remaining years of life

DELIRIOUS REACTIONS

A delirious reaction may be defined as a reversible psychosis marked by disorientation hallucinations and fear It may be the sole mental disorder or may be superimposed on a more serious mental disturbance or psychosis Included in the term are the so called exhaustion and toxic psychoses In old persons the cerebral circulation through the narrowed sclerotic arteries is often just adequate to maintain the normal function of the brain Any slight disturbance may upset the balance and lead to transient anoxemia or other damage to the brain cells Operation trauma infection heart failure cachexia sudden dehydration with mercurial diuretics and protracted administration of sedative drugs such as the bromides and barbiturates may induce delirious reactions At times prolonged malnutrition or diets lacking in vitamin content may induce a pellagra like psychosis The insecurity and the natural anxiety of the patient often form the basic psychological background of the delirious reaction

Delirious reactions are common in older patients Doty[13] encountered them in 15 per cent of patients over 40 seen as a psychiatric consultant in a large general hospital Robinson[14] reported that 20 per cent of all patients over age 60 ad

[13] Doty E J Incidence and Treatment of Delirious Reactions in Later Life Geriatrics 1 21 Jan Feb 1946

[14] Robinson G W Jr "The Toxic Delirious Reactions of Old Age" in Kaplan O J (ed) *Mental Disorders in Later Life* (Palo Alto Calif Stanford University Press 1945)

mitted to a neurological hospital had delirious reactions and that an additional 20 per cent had delirious reactions super imposed on some other type of mental reaction Symptoms may come on suddenly the patient may be drowsy in the daytime but soon grows restless especially at night and his frightening dreams Soon he loses his orientation becomes fearful and develops hallucinations and then delusions which may have a paranoid trend Bodily tremors and incoordination as well as urinary incontinence develop the patient becomes noisy and uncooperative Unless vigorous treatment is instituted, dehydration and malnutrition develop and aggravate the mental disturbance Death may follow With a favorable outcome the delirium may last from a few days to weeks

Treatment —In the presence of complicating disease the underlying condition should be treated Infection should be combated heart failure corrected and the diet made adequate Feeding by stomach tube to assure a high calorie diet is often necessary Intravenous administration of fluids to correct dehydration is important and glucose and amino acids may be given by this route Large doses of vitamins should be given parenterally if necessary Particularly important is nicotinic acid which should be given in doses of 100 mg three times a day for a week or two Secondary anemia should be treated with iron or if necessary, with transfusion Sedatives should be avoided as much as possible The bromides and the barbiturates often aggravate the delirium If quieting drugs are needed morphine may be employed or scopolamine in a dosage of 1/150 gr three ti day Continuous baths may be quieting

Intelligent vigorous therapy often cures the mental d ance It is well to remember that nutritional and to ments may superimpose delirious reactions on a tr

and arteriosclerotic psychosis and that treatment such as that just outlined may salvage the mentalities of many of the aged who in former years would have been allowed to become senile derelicts Robinson[15] reported 60 per cent complete re coveries among patients of 60 or more who were admitted to a hospital for mental diseases with severe abnormal mental reactions Most of them had remained well when checked six months later

PSYCHOSES

Mental disorders become increasingly frequent with ad vancing years A study in Massachusetts[16] showed that while about 2 per cent of the population between the ages of 30 and 60 in that state were admitted to mental hospitals a much greater proportion of persons over 60 entered these institutions the frequency increasing with each decade Thus about 3 per cent of the male population of Massachusetts between the ages of 60 and 69 5 5 per cent of those 70 to 79 and 8 5 per cent of those 80 to 89 years of age were admitted to mental hospitals The frequency of mental disease in wo men is somewhat lower than in men but the same increasing prevalence with advancing years is evident Thirty per cent of the patients admitted to the state hospitals for mental dis eases in New York State are over the age of 60 Not all of these suffer from senile or from arteriosclerotic dementia There are those with toxic psychoses with manic-depressive psychosis and with paresis About 9 per cent of persons on first admission have senile psychoses and again as many have psychoses secondary to arteriosclerosis of the cerebral arteries

15 Robinson G W Jr "The Abnormal Mental Reactions of Old Age" J Missouri M A 39 36 February 1942

16 Dayton N A *New Facts on Mental Disorders* (Springfield Ill Charles C Thomas Publisher 1940)

The chief psychoses encountered in older persons are the involutional psychoses senile psychoses and psychoses with cerebral arteriosclerosis Their relative frequency and age distribution are shown in Table 8

TABLE 8 —Rates of First Admissions to All Hospitals in New York State per 100 000 of General Population of Same Age 1942

Ages	Senile Psychoses		Psychoses with Cerebral Arteriosclerosis		Involutional Psychoses	
	M	F	M	F	M	F
50 54	1 1	0 5	20 0	20 3	16 9	57 3
55 59	2 1	3 8	53 1	47 2	14 7	43 8
60 64	8 1	15 1	107 6	94 4	12 8	18 5
65 69	33 0	54 9	199 9	168 1	3 7	11 1
70 and over	254 9	311 1	333 8	264 1	0 8	1 4

Adapted from Pollock in Kaplan O J (ed) *Mental Disorders in Later Life* (Palo Alto Calif Stanford University Press 1945)

INVOLUTIONAL PSYCHOSES

Involutional psychosis or melancholia is three times as frequent in women as in men Its age of occurrence is between the years 45 and 55 in women and about a decade later in men Its cause cannot be found in the hormonal changes that accompany the climacteric although in some cases these may contribute to the disorder Apparently constitutional factors are of great importance Persons who develop this psychosis have rigid repressed personalities They display obsessional characteristics a surrender to meticulous detail Environmental factors that become operative at the time of life when the psychosis develops may play a role in its development The patient has reached a period when further advance is difficult he may realize that he is a failure he cannot adjust to financial reverses or other stresses such as the death of close relatives and friends

Prodromal symptoms of depression irritability and loss of weight with feelings of unreality and a tendency to withdrawal from the environment may extend over several years Finally the depression overwhelms the patient in full force but it is associated with anxiety and with motor overactivity or agitation Delusions of unworthiness and of sin and self accusation with well marked suicidal trends are prominent There are ideas of death of poverty religious delusions and auto erotic preoccupations There may be somatic delusions varying from hypochondriasis to the conviction that all of the organs have been lost There may be little disturbance of consciousness and orientation Paranoid trends may develop

The psychosis runs a prolonged course and the outlook for recovery is not good particularly in persons over 55 years of age in those with compulsive trends and in patients who in their youth exhibited great rigidity and narrow mental horizons Approximately one quarter experience a spontaneous recovery one fifth die by suicide or intercurrent disease and most of the others remain ill

If the condition is recognized in its prodromal stages much may be done by helping the patient adjust to his environment by correcting any existing physical disorders and possibly by substitution therapy with estrogenic or androgenic hormones When the psychosis is fully developed institutional treatment usually becomes necessary particularly because of the risk of suicide Full use should be made of hydrotherapy and occupational therapy and skilled and understanding nurses should be in continuous attendance The patient is usually resistant to psychotherapy Treatment with estrogenic hormone and with testosterone has been disappointing although it may be a useful adjuvant

Today electric shock treatment seems to hold out the best hope and many good clinical results have been reported

especially in patients with recent cases and in patients in whom schizoid personalities and paranoia are not prominent features Age in itself is no contraindication to electric shock therapy unless there is severe cardiovascular impairment Such treatment has a distinct field of usefulness in many patients past 65 who have depressive manic or paranoid psychoses conditions that ordinarily do not yield to other forms of therapy [16] I have seen it bring about remarkable improvement in an 80 year old woman with a marked paranoid psychosis Some few patients show intellectual deterioration as a result of treatment Electric shock therapy should not be employed for senile dementia

SENILE PSYCHOSES AND PSYCHOSES WITH CEREBRAL ARTERIOSCLEROSIS

Senile and arteriosclerotic psychoses and dementia are by definition caused by regressive or vascular irreversible changes in the brain They are organically conditioned Yet old persons who have died without any mental impairment may have brain lesions as severe as those seen in individuals who have died with senile or arteriosclerotic psychoses There is no close correlation between the intensity of the mental symptoms and the extent of the cerebral pathological changes found at autopsy [17] In this respect the brain resembles the heart and other organs in which a close parallelism between structural and functional alterations can rarely be established Just as the damaged heart compensates for its structural weakness and maintains the circulation but becomes

[16] Feldman F et al Electric Shock Therapy of Elderly Patients Arch Neurol & Psychiat 56 158 August 1946

[17] Rothschild D Senile Psychoses and Psychoses with Cerebral Arteriosclerosis" in Kaplan O J (ed) *Mental Disorders in Later Life* (Palo Alto Calif Stanford University Press 1945)

insufficient if it is subjected to too great physical strain so the scarred and atrophic brain compensates and maintains a normal cerebral and emotional pattern for the aging person by bypassing its scarred structures and using other nervous pathways for co ordination Severe emotional shock the death of husband or wife the loss of home any assault on the security and integrity of the individual may overtax these compensatory mechanisms so that a breakdown of cerebral function ensues Severe anatomical damage to the brain will induce mental disorders in anyone but in most instances they are the personal and environmental factors overloading a damaged cerebral mechanism that lead to the mental break down

Senile dementia characterized by a slowly progressive but inexorable intellectual impairment becomes manifest on the average at age 75 It is more frequent in women than in men The pathological picture is not pathognomonic similar but less pronounced lesions are seen in the brains of aged per sons who have died with their mental faculties intact There is a diffuse but spotty cortical involvement with atrophy of the nerve cells Yet the cortical architecture is preserved There is a proliferation of the microglia and macroglia and many senile plaques are evident

The psychosis usually develops slowly and manifests it self at first by a variety of neurasthenic complaints weakness alterations in habits of sleep and growing irritability and emotional instability It may be precipitated by serious emo tional traumas occasioned by the death of a close relative loss of income or security or the development of some serious organic disease such as cancer Soon intellectual deficits be come apparent the patient becomes forgetful especially of recent events and his judgment and mental acuity are im paired Memory defects may lead the patient into dangerous

situations He may wander from home and become lost he may set himself or his house on fire by the careless handling of matches and stoves There are diminution of attention and lack of sympathy for and understanding of others the patient becomes self centered stubborn depressed or euphoric The old person exhibits in his psychosis his own lifetime personality and many of his reactions are falsely attributed to old age He lives in the past may indulge in fabrications and be loquacious in his reminiscences Defects in orientation develop and eventually there is marked mental confusion the patient becomes neglectful in matters of dress eating and cleanliness Loss of moral judgment may lead to asocial acts Anxieties such as fear of poverty or of personal harm may develop Some especially persons who have had suspicious natures in their younger years may exhibit a paranoid form of dementia In these there may at first be little impairment of memory or of intellectual functions but eventually they too present the picture of progressive mental deterioration Others exhibit periods of excitement or agitation or euphoria and may develop abnormal sexual activity In time deterioration becomes complete with progressive weakness emaciation and incontinence of the sphincters The patient is in a helpless vegetative state which is terminated by death The average duration of life after the onset of symptoms is 4 7 years and after admission to a mental hospital 1 7 year

Arteriosclerotic dementia bears no direct relationship to aging It is the result of repeated cerebrovascular insults that lead to progressive destruction of brain tissue Like arteriosclerosis it is more common in men than in women The average age at onset is 66 years and the average duration of life after the development of symptoms is 3 4 years The pathological lesion is characterized by vascular changes with

focal areas of destroyed brain tissue Areas of softening and of hemorrhage are found especially in the basal ganglia and the temporo occipital regions There are atherosclerosis of the larger cerebral arteries and arteriolosclerosis with hyaline degeneration of the smaller vessels The patient commonly exhibits coronary and aortic sclerosis hypertension hemiplegia or other palsies tremors and aphasia In the psychoses with cerebral arteriosclerosis there is the same lack of correspondence between evident damage to the brain and mental symptoms that is encountered in senile dementia Here too psychotic symptoms are more frequent and more prominent in persons who have previously had abnormal personalities

The mental manifestations are much the same as those in persons with senile dementia but the patient also exhibits symptoms and neurological signs resulting from cerebral injury The psychosis is often precipitated by a cerebrovascular accident there is sudden onset of confusion or delirium which may persist for weeks or months and which ends in death in half the cases In others the mental disturbance subsides but the patient complains of headache and dizziness syncopal attacks or convulsions are common and apoplectic seizures or attacks of heart failure recur With each such episode there are further damage to the brain and further mental deterioration Intellectual impairment as a rule is not as pronounced as in senile dementia and there may be marked fluctuations in the degree of intellectual disturbance Acute states of confusion or depressive symptoms are common in arteriosclerotic psychoses Death results from the arterial disease cerebral hemorrhage renal insufficiency or cardiac failure

Treatment of senile and arteriosclerotic dementias is not very fruitful It concerns itself with general hygiene the

maintenance of nutrition and the establishment of a favorable environment When there is marked depression or agitation or when the patient becomes a social problem because of his amoral actions or because of extreme untidiness, institutional care becomes necessary Vigorous treatment of the organs damaged by the arteriosclerotic arteries, particularly treatment of cardiac and renal failure, has a favorable influence on the mental condition If the blood pressure is high, phlebotomy is useful

The *presenile dementias* present themselves chiefly in two forms[18] Alzheimer's disease begins between 40 and 60 and although symptoms develop rapidly its course runs from two to 10 years The clinical picture resembles that of senile dementia but, in addition there are aphasia, agnosia, apraxia tremors and rigidity Epileptiform seizures are common The air encephalogram reveals diffuse cortical atrophy with enlargement of the lateral ventricles The pathological picture resembles that of advanced senile dementia but the so called senile plaques are numerous and there are characteristic changes in the intracellular neurofibrils Pick's disease may begin in the sixth or seventh decade and is often familial in its occurrence It is characterized by slowly progressive dementia with focal cortical signs such as aphasia agnosia and apraxia The brain shows circumscribed areas of atrophy of the gray and white matter confined to one or more lobes During life these atrophic areas can be recognized in the air encephalogram

The suicide rate increases progressively with advancing years One half of all suicides occur in persons 45 years of age or older although this age group constitutes only one fifth

[18] Jervis G A The Presenile Dementias in Kaplan O J (ed) *Mental Disorders in Later Life* (Palo Alto Calif Stanford University Press 1945)

of the total population The suicide rate per 100 000 in white males is 30 at age 40 43 at age 50 57 at age 60 63 at age 70 and 80 at age 86 For females the incidence is much lower and the progressive increase with the years is less evident The rate per 100 000 at age 40 is 8 and between the ages 50 to 80 it remains fairly uniform at about 10[19] Negroes have a much lower suicide rate than do whites

Often medicolegal problems arise regarding the mental competency of the aged This may relate to the making of financial transactions or more often of a will Sexual transgressions such as exhibitionism or attacks on children loss of a sense of values and lack of judgment leading to financial irregularities in persons of previous integrity may be first evidence of senile deterioration It is important that the family practitioner make a written record of his observations of the mental reactions of his old patients just as he does of their physical ailments Such notes may be of great service if legal problems should arise

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[19] Dublin L I and Bunzel B *To Be or Not to Be A Study of Suicide* (New York City Harrison Smith & Robert Haas 1933)

the regions of skin used in most of these experiments do not contain any receptors which appear 'structurally specialized under the light microscope (Ecker and Wiedershein, 1896)

Specificity has been shown directly by looking for activity in single receptor units while testing the sensitivity of their receptive fields with a variety of stimuli In the early work activity in individual nerve fibres was distinguished by differences in the size and shape of individual action potentials which could be seen while recording from a small bundle of fibres, differences in conduction velocities gave indirect information about the diameter of the fibres (Adrian, 1931, Hogg, 1935, Zotterman, 1939) More recently Maruhashi, Mizuguchi and Tasaki (1952) *have dissected single fibres from cutaneous nerves* The results of all these experiments, and many similar ones by other workers, show that every unit has a particular pattern of sensitivities Usually a unit is highly sensitive to one type of energy and much less sensitive to other types There are, however, exceptions, for example the pit organ of certain vipers is highly sensitive to both mechanical and thermal energy (Bullock and Diecke, 1956) In all these experiments the output of the receptor unit was recorded with the unit *in situ*, this must be remembered, since experiments of this kind cannot indicate whether the specificity is determined by the properties of the supporting tissues or by the biological transducer itself They can, however demonstrate that receptor units *in situ* can be distinguished by their specific patterns of sensitivity This conclusion is at present only a qualitative one and further work is required to establish the relative quantities of various types of energy needed to excite receptor units

Distinctions between energy types are normally detected by the nervous system because receptor units show big differences in their sensitivities to different types of energy distinctions within an energy type, however often depend on an analysis of overlapping sensitivities For example Hensel and Zotterman (*see Zotterman, 1953) described two types of temperature* sensitive unit in the cat s tongue For both units the curve relating impulse frequency to temperature is of a humped type, the frequency decreasing as temperature rises above or falls below

the optimum value the difference between the two types of unit is that the peaks of the curves occur at different temperatures (Figure 1) The curves are quite repeatable so that a particular temperature of the receptor is always associated with a particular frequency of impulses in the nerve, but, a particular

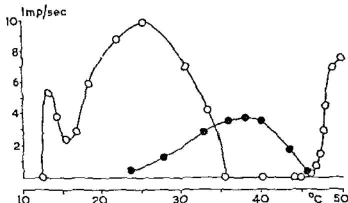


FIGURE 1 Impulse frequency against temperature curves for two types of thermal receptor from cat s tongue (From Zotterman 1953)

frequency of impulses is not uniquely related to one temperature because, except at the peak of the hump there must be at least two temperatures both of which are associated with the same frequency in any one unit (Figure 1) The curves of the two types of unit overlap and this overlap is sufficient to ensure that any pair of frequencies in a pair of units uniquely relates to a particular temperature in the working range, the increase in frequency found at high temperatures in those units which normally respond at lower temperatures, is outside the normal working range Another example of this type of overlap may possibly occur in relation to human colour vision (see Thomson 1952) The sensation aroused by a light has three independent qualities its brightness its hue and its saturation, it can be shown experimentally that only three quantities need be controlled in order to give rise to a range of sensations which include all possible colours at all levels of brightness Any further variability in the experimental apparatus is redundant It therefore appears that there are only three independent mechanisms

in the nervous system associated with colour sensation, this limitation to three need not occur in the receptor units, though it is clear that there cannot be less than three independent mechanisms at this level Curves relating the sensitivity of each of the three postulated mechanisms to different wavelengths of light have been deduced, they show peaks at different wave lengths and almost complete overlapping In theory a particular activity in each of these three mechanisms gives a unique combination which can determine all three properties of the sensation

A different type of overlapping of sensitivities has been described by Pfaffman (1941) as occurring among the chemo receptors of the tongue of the cat He described four types of unit, one, for which the evidence was a little uncertain could be excited with sucrose, of the other three, one was sensitive to acids and simple salts, one to acids and quinine and the third only to acids All the information required to distinguish acids, salt and quinine can be transmitted by simple combinations of these units This type of organization has much in common with that concerned with spatial discrimination, and the principles involved will be discussed below

Receptive fields

The area in which the receptors of a single unit lie is known as the receptive field of that unit, these vary in area from points up to large sizes, the largest recorded being 45 cm ² (Adrian, Cattell and Hoagland 1931 Maruhashi *et al* 1952) In general the receptive fields of neighbouring receptor units overlap to a great extent and such overlapping is found not only in skin, but in eyes and, in a somewhat different form, in the mammalian cochlea There is a theoretical advantage in the overlapping of receptive fields if the localization of a single stimulus is the principal objective an area supplied by a number of receptor units can be represented as a mosaic of small areas each of which is supplied by a particular and unique combination of units (Figure 2) The number of such small areas will be the number of combinations that can be made from the number of units available, for example, the fields of three receptor units over lapping in a regular manner would give seven distinguishable

areas However, the total number of units required depends on the total amount of information to be transmitted and this may include factors other than the localization of a single stimulus for example the overlapping organization could theoretically increase localization at the expense of discrimination between simultaneous stimuli

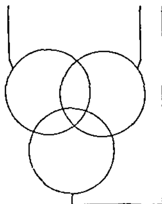


FIGURE 2 Diagram to illustrate seven combinations from three overlapping receptor fields

Activity in units

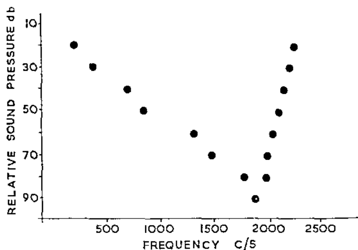
The intervals between the impulses travelling in the nerve fibre of a receptor unit depend on the stimulus strength This well known fact first observed by Adrian and Zotterman (1926) needs a little amplification in the context of the subject of this lecture In many instances stimulus can be taken to mean some factor that is independent of time say temperature or force and in these instances a particular value of the stimulus is related to a particular frequency of nerve impulses good examples of this are to be found in the relation between temperature and frequency for two types of unit in the cat s tongue (see Zotterman 1953) (Figure 1) and in the relation between impulse frequency in units from the cat s carotid sinus and the pressure in it (Landgren 1952) A stimulus need not however be *independent* of time Probably *all* units that signal steady states also respond and with even greater sensitivity to changes of state furthermore a large number perhaps a majority of

in the nervous system associated with colour sensation this limitation to three need not occur in the receptor units, though it is clear that there cannot be less than three independent mechanisms at this level Curves relating the sensitivity of each of the three postulated mechanisms to different wavelengths of light have been deduced, they show peaks at different wave lengths and almost complete overlapping In theory a particular activity in each of these three mechanisms gives a unique combination which can determine all three properties of the sensation

A different type of overlapping of sensitivities has been described by Pfaffman (1941) as occurring among the chemo receptors of the tongue of the cat He described four types of unit, one for which the evidence was a little uncertain, could be excited with sucrose, of the other three, one was sensitive to acids and simple salts, one to acids and quinine and the third only to acids All the information required to distinguish acids, salt and quinine can be transmitted by simple combinations of these units This type of organization has much in common with that concerned with spatial discrimination, and the principles involved will be discussed below

Receptive fields

The area in which the receptors of a single unit lie is known as the receptive field of that unit these vary in area from points up to large sizes, the largest recorded being 45 cm ^{2} (Adrian, Cattell and Hoagland, 1931, Maruhashi *et al* 1952) In general the receptive fields of neighbouring receptor units overlap to a great extent and such overlapping is found not only in skin, but in eyes and, in a somewhat different form, in the mammalian cochlea There is a theoretical advantage in the overlapping of receptive fields if the localization of a single stimulus is the principal objective, an area supplied by a number of receptor units can be represented as a mosaic of small areas each of which is supplied by a particular and unique combination of units (Figure 2) The number of such small areas will be the number of combinations that can be made from the number of units available, for example, the fields of three receptor units overlapping in a regular manner would give seven distinguishable



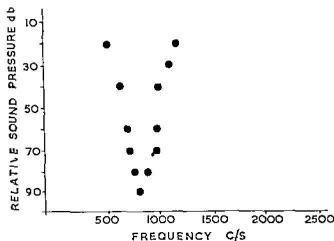


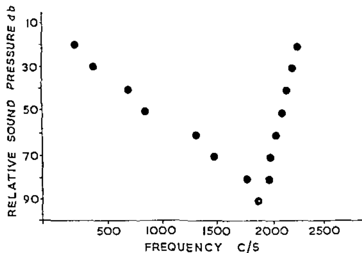
FIGURE 3 Intensity of sound pressure for a constant response at different sound frequencies (*a*) for a single primary receptor unit (*b*) for a single secondary unit of the cochlea nucleus (Redrawn from Sumi Katsuki and Uchiyama 1956)

units, respond only to changes of state This is not surprising since, if the nervous system had a good enough 'memory, it would be quite unnecessary to have receptor units signalling steady states, only the changes would have to be recorded When considering organization *in situ*, frequency cannot be regarded as an independent measure of intensity, thus a low level of activity in a mechanically sensitive unit could indicate either a small force applied to the skin locally or a large force applied at a distance A good example has been found by Tasaki (1954) in the cochlea, a single unit will respond to a wide range of frequencies of sound waves but, for a given sound intensity, the frequency of impulses will be different at each frequency of sound, in other words the frequency of impulses in any one unit may be altered either by a change of intensity or a change in the frequency of the sound The information carried by a single unit cannot, therefore, enable a distinction to be made between a change in one or the other of these quantities, two units with different frequency sensitivities are therefore required

Analysis

The main theme of this lecture has been that there are a number of variables available for the transmission of information in the peripheral nervous system, but these variables are not necessarily each associated with a specific type of information Thus there may be overlap in the specificity of the unit and also spatial overlap of the receptive fields There can also be interaction between the intensity and other characteristics of the stimulus if the activity of a unit *in situ* is considered It has been pointed out that no information is lost by this overlapping organization provided that the nervous system is able to make the necessary analysis An analysis must obviously be made and recent work on the mammalian cochlea (Galambos, 1944) retina (Barlow, 1953, Kuffler, 1953) and arthropod eye (Hartline Wagner and Ratliff 1956) has suggested that this analysis begins at a low level in the nervous system, probably at the first synapse

An example may be used to illustrate this point In the mammalian cochlea it has been shown that the displacements of the



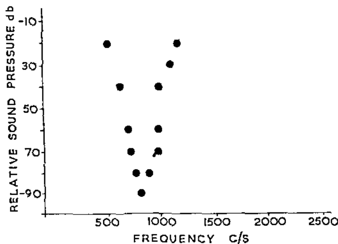


FIGURE 3 Intensity of sound pressure for a constant response at different sound frequencies (a) for a single primary receptor unit (b) for a single secondary unit of the cochlea nucleus (Redrawn from Sumi Katsuki and Uchiyama 1956)

XXI

Poliomyelitis

G W A DICK

It is not my intention to review all the recent advances in the field of poliomyelitis and I shall discuss only the natural history of the virus, and the effects of vaccination Those are two aspects of poliomyelitis research on which my team in Belfast—Drs Dane, Connolly, Likar and Mr McFerran—have been engaged over the past few years and to much of whose work I shall be referring

Although poliomyelitis is as old as history it was sporadic and relatively rare until the end of the nineteenth century when it appeared as an epidemic disease in Scandinavia and North America What change occurred in the biological relationship of the virus and the host to make poliomyelitis an epidemic disease?

In London, e g prior to 1947, epidemics of poliomyelitis were unknown What happened in London or Berlin in 1947 to make the disease epidemic? (Figure 1) Was a virulent virus imported? Did something happen to a virus which had been present in the community for many years? Was there a host or environmental change to upset the previous relatively stable equilibrium, or had this 1947 epidemic something to do with the weather?

Now it is rather surprising, although poliomyelitis has been more studied over the past ten years than any other infectious disease—studied with elaborate tissue culture and animal techniques—that we know really very little more about the natural history of the virus than did Wickman (1913) or Gardner Robb (1916) more than forty years ago

Briefly what do we know? We know that there are three types of poliovirus, types 1, 2 and 3 and that type 1 is responsible for about 80 per cent of all paralytic infections We know that the disease is spread by person to-person contact and that epidemics



FIGURE 1 Showing cases per 100 000 in London 1932–47 and Berlin 1928–47 (From Sabin 1949)

of paralytic poliomyelitis occur in the late summer and autumn months in temperate climates We also know that infections with polioviruses are a common experience not usually manifest through any recognizable illness that infections at a clinical or subclinical level result in resistance to further attacks that the incidence of clinical disease is inversely proportional to the incidence of infection and, in general that the incidence of clinical disease is increasing in countries where infection is declining

It will soon be very obvious what we do not know and I am afraid much of this lecture will be devoted to pointing out some of the unknowns

Natural History

In considering the natural history of any parasite we must remember that its survival depends on its ability to fulfil the following requirements (a) to make an entry to the host, (b) to multiply in the host, (c) to make an exit, and (d) to reach a new host Let us consider each of these in relation to poliovirus

Entry of virus

The virus is primarily an enteric one and it is reasonable to assume that the natural portal of entry is the mouth Further more, natural infections can be initiated experimentally in man by the oral route While infections can be produced by paren teral inoculation there is no evidence that this mode of entry plays any part in the natural history of the disease When man is inoculated intramuscularly with an attenuated type 3 strain of poliovirus (Sabin, 1955) or accidentally with poliovirus, virus reaches the gut and multiplies there

Multiplication of virus

Where then does the virus multiply after making its entry by the mouth? Although virus can be recovered from the throat secretions of some individuals during the early days of infection and also from the throat of individuals who have been fed large quantities of live virus, multiplication of the virus in the throat does not always occur and it is not a necessary precursor of infection of the gut The exact site of virus multiplication in the gut is not yet certain but the measure of this multiplication in humans is obtained from the amount of virus excreted in the faeces

Studies with live virus vaccines which we have made in Belfast (Dane, Dick, Connolly Fisher and McKeown 1957 Dick, Dane Fisher Connolly and McKeown 1957) by feeding types 1 and 2 polioviruses, have shown that there are great variations in the patterns of virus excretion by different individuals In the first place there is a very great difference in the facility in which virus multiplies in children as compared with adults After feeding a type 2 virus to individuals who were

devoid of poliomyelitis antibody, we found that none of 10 adults excreted detectable virus while 15 of 18 children (83 per cent) did so for variable periods The quantity of virus excreted by the children varied enormously and there were also very great variations in the duration of virus excretion In all children whom we have studied all who excreted virus developed anti body, those who did not excrete virus did not develop antibody, whereas 3 of the 10 adults who did develop antibody did not excrete detectable virus

It was found that the younger the child the greater is the excretion of virus We have also observed that in general the family pattern of virus excretion is similar in all siblings of a family Some families seem to be good excretors of virus and some families are poor excretors We have several families in which the children failed to excrete virus at all after virus feed ing Failure to excrete virus or develop antibody by one sibling was usually associated with a similar failure in the other sib ling(s)

To summarize these findings we have evidence that (a) virus multiplies better in the alimentary tract of children than of adults, (b) virus multiplies better in younger children than older children (c) resistance and susceptibility of the gut to poliovirus infection seems to be family tied

Exit of virus from host

How does the virus make its exit from host? It is obviou that one site of exit is the lower end of the alimentary tract Does virus also make an exit from the mouth? We do not think that this is a common occurrence

The evidence implicating the oropharynx as an important site of exit of virus may be briefly summarized as follows (a) virus has been isolated from the pharynx for various times within a week before onset of symptoms of the major illness and for 3–4 days after (b) virus has been isolated from the stools from 12–19 days before the onset of illness and for many weeks after (c) the period during which virus has been isolated from the pharynx coincides with the calculated infectious period (arrived at from single contacts) as shown diagrammatically in Figure 2 It seems

TABLE 1 Showing spread of poliovirus within a amily after feeding one child with an oral type I vaccine virus

+ = > 10² ³tcd₅ per gm faeces – = < 10² ³tcd₅₀ per gm faeces		Days after feeding virus (0 7 14 21 28)	Antibody 6 weeks after
Female—4 years Antibody < 1 4 Fed virus (S M)	Throat virus	– – – – – – – –	1 256
	Faecal virus	+ + + + (6 5*) + + (2 3) – – –	
Contact Male—2 years Antibody < 1 4	Faecal virus	– – – – + + (4 8) + (5 6) – – – –	1 32

* Where a specimen has been titred log₁₀ of titre per gm is given

reasonable to assume that there is a biological relationship between pharyngeal virus and infectiousness and the fact that the continued excretion of virus in the faeces has not been associated with late secondary cases seems to support this view

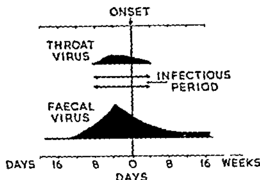


FIGURE 2 Diagram showing excretion of faecal and throat virus in relation to infectious period.

What then is the evidence indicating that infection may not depend on oropharyngeal virus? In the first place we have direct evidence that person to person spread can occur in the absence of any demonstrable virus in the throat A study which we made in a doctor's family is summarized in Table 1 All members of the family were devoid of type 1 antibody when the girl, aged 4 years was fed with an attenuated type 1 strain of poliovirus She excreted virus in the stool for about a week, but no virus was recovered from her throat in daily swabs yet this child infected her young brother by contact Although virus is often found in the throat for a few days during the incubation period and early days of infection, it is very rarely found in the saliva or in swabs of the anterior part of the mouth With one exception we have repeatedly failed to recover virus from the mouth or lips of individuals who were excreting virus in the throat We have little information on the quantity of virus present in the throat but it is considerably less than the 'peak titres which we and others have found in faeces Indeed, the greatest amount of virus we have observed in the throats of naturally infected individuals has been more than one hundred

times less than what is commonly found in faeces In all our studies we have found that the 'peak titres' of faecal virus excretion occur during the first week or 10 days after infection, and similar observations have been made by others This period of maximum virus excretion also corresponds with the estimated period of infectiousness (Figure 2) and also with the experimentally observed period of infectiousness (Table 1)

Infection of new hosts and spread in the community

The type of contact among children which will produce a faecal oral infection is similar to the kind of contact which will produce a pharyngeal oral infection You just want to watch a group of children at play to convince yourself of this The important factor in transmission is of course intimate contact among children I doubt whether it will ever be possible to define the relative importance of oropharyngeal or faecal oral transmission but I personally think that the high titre faecal virus in the early days of infection is the most important means of spread, and that children are the most important disseminators of virus

It is now well established that if one child in a family becomes infected other members of the family will also be infected and that the rates of clinical poliomyelitis are greater among family or household contacts of a poliomyelitis case than among the remainder of the population Thus, Paffenbarger, Wilson, Bodian and Watt (1954) in an analysis of contact during epidemic periods have shown that the rates of poliomyelitis were 2 to 5 greater among contacts than among the remainder of the population *A similar type of study by* Horstmann, McCollum and Mascola (1955) showed that the ratio of clinical to inapparent infections among family contacts was 1 7 as compared with an estimated figure of 1 100 in the general community It seems therefore, from these and similar studies of this type that paralytic poliomyelitis breeds paralytic poliomyelitis How can one explain this? There are several possible explanations but the most likely seems to be as follows In the family studies which I have mentioned the families and contacts were picked up only because a paralytic case had

occurred in the family Now I have already mentioned the variation in virus excretion by different families In some families virus multiplies well while in others it multiplies poorly It seems to us that families in which a paralytic case occurs may be families in which virus multiplies well They may be regarded as hot families, not only from the point of view of having a case but also from their ability to transmit paralytic polio myelitis and it would seem that such families may be con sidered to be epidemiologically dangerous Other families may be regarded as cold families unlikely to have clinical polio myelitis because the virus multiplies poorly in them, and un important in transmission, to any but their closest contacts, because they are poor excretors of virus Some years ago Bradley (1950) from epidemiological studies, suggested this concept of the spread of the disease—that is that paralytic poliomyelitis as opposed to poliomyelitis infection appeared to spread through the community in a narrow stream I disagreed with him at the time but from experimental evidence now available I think he was right One can then visualize an epidemic of polio myelitis spreading through a community as shown dia gramatically in Figure 3

We have no idea why families behave in these different ways nor do we know why some members of some families become paralysed while others do not It appears however, that viraemia is a frequent and probably regular event in families in which an index case has occurred and that viraemia is a pre cursor of paralysis This does not mean that everyone who gets poliovirus in the blood stream will get paralysed but it may be that in those families in whom virus multiplies well there is more viraemia which increases the opportunity for the virus to break the blood brain barrier and get to target areas in the CNS It appears then that there are some families who are important in the transmission of the paralytic disease and that these may be the families in whom paralytic cases occur We think therefore that if a paralytic case occurs in a family we must regard the paralytic child and siblings of that family as most important disseminators of virus We believe that the siblings in such a family should have household quarantine for

7–10 days, i e during the period when they will be excreting large quantities of virus By this time they may have already transmitted the virus to their friends, but this does not mean that such quarantine will always be useless

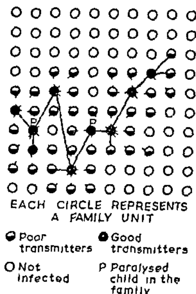


FIGURE 3 Diagrammatic representation of the spread of a virulent strain of poliovirus in a community

Epidemic character of poliomyelitis

How then can we explain the epidemic character of polio myelitis? I am going to consider only one situation—the appearance of epidemics in countries where poliomyelitis is endemic Why for example did polio suddenly become epidemic in London and in Berlin in 1947? (Figure 1) Why in 1945 did a poliomyelitis epidemic suddenly hit the island of Mauritius? Most people thought that a virulent virus had been imported, but our studies (McFarlan Dick and Seddon 1946) led us to believe that poliomyelitis was endemic in Mauritius Just before the epidemic broke out there was a severe cyclone and we con cluded that perhaps as a result of the cyclone, to use a phrase of Andrewes (1940) the virus had 'got its teeth

Let us take another example—from Northern Ireland In Belfast, as shown diagrammatically in Figure 4 there were 19 paralytic cases in 1952, 31 in 1953, 14 in 1954, 1 in 1955 and 7 in 1956 While in 1957 there were 98 paralytic cases How does

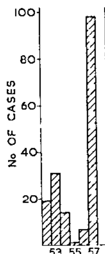


FIGURE 4 Cases of paralytic poliomyelitis in Belfast 1952–7

one explain this 1957 epidemic? Can it be explained quite simply by the building up of a sufficient number of susceptible individuals in the community as in measles with epidemics appearing every few years? This would imply that there is a *relative* absence of type 1 virus in the community in non epidemic years We know that type 1 virus *is* present in Northern Ireland in non epidemic years as evidenced by the recovery of virus from scattered cases Can we explain the epidemic picture then as mainly due to the emergence of sus ceptible children? I do not think that this is at all likely for I think that type 1 infections are occurring at a fairly constant rate within the community from year to year It is difficult to prove this conclusively but there is some evidence to support it, such as the studies of type 2 antibody by Turner Hollander Buckley Kokko and Winsor (1950) who showed that in Balti more the rate at which infection was acquired remained relatively high year after year regardless of the occurrence of

epidemics of clinically recognizable poliomyelitis It appears then that at least in some communities polioviruses are spreading at a fairly constant rate every year Why then do epidemics of paralytic disease occur? Is it possible that there is no change in the prevalence of infection from year to year but that there is a change in the parasite, or in the host, during epidemic years, which leads to a greater proportion of paralytic cases to silent infections?

A change in the parasite could mean either that a virulent strain is imported, perhaps from Scandinavia or North America the homes of epidemic poliomyelitis—and many people have put epidemics down to this—or else what appears to us to be more likely—that a change has occurred in the endemic strains

Comparison of virus strains

If epidemic strains differed from endemic strains, we thought that it might be possible to show that strains causing paralysis during epidemic years are different from strains which are silently immunizing a community at the cost of an occasional sporadic paralytic case, i e it might be possible to show that viruses recovered during epidemic years were of different virulence from endemic strains The only satisfactory index of the virulence of polioviruses is their neurotropism for monkeys inoculated intracerebrally (i c) So we began to test the monkey neurotropism of type 1 strains recovered in Belfast from sporadic cases of paralysis during a non epidemic year and to compare them with strains from individuals paralysed during the 1957 epidemic All specimens were tested in a similar way and the viruses were inoculated i c into monkeys So far we have studied 3 epidemic and 4 non epidemic strains from paralysed individuals and we can show no difference in the virus from paralytic cases occurring in non epidemic and epidemic years It did not seem likely therefore, that a highly virulent strain had been imported during the epidemic year

As part of this study of strains, which is still in progress, we are comparing the monkey neurotropism of strains from paralysed children and their asymptomatic contacts The comparisons of one such pair is shown in Table 2

During the 1957 epidemic, virus was recovered from a paralysed child and his non paralytic and asymptomatic contacts at a small nursery school The viruses from the paralysed child and one of the asymptomatic contacts were inoculated in comparable amounts into monkeys In Table 2 the paralytic ratios

TABLE 2 Showing comparison of monkey neurotropism of type I polioviruses recovered from faeces of a paralysed child and an asymptomatic contact at a nursery school

TCD_{50} (logs) of virus inoculated	Paralytic ratios of rhesus monkeys inoculated intracerebrally with 1st tissue culture pass of type I virus from	
	Paralysed child	Asymptomatic child contact
2	0/3	—
3	1/3	0/3
4	3/3	0/3
5	3/3	1/3
6	3/3	1/3

of monkeys inoculated with 2 logs—100 tissue culture $doses_{50}$ (TCD_{50}), 3 logs i e 1 000 TCD_{50} and so on up to 6 logs or 1,000 000 TCD_{50} of each virus are recorded As the results show, the paralysed child was excreting a much more virulent virus than his asymptomatic contact, as indicated by the proportion of paralysed monkeys at each dilution

The two possible ways of explaining this result are either (a) that there were two strains of virus—one virulent and the other avirulent spreading in the nursery school at the same time or else (b) that there was only one strain which was capable of rapid change from virulence to avirulence or *vice versa* We have evidence that human beings can very readily change the virulence of a poliovirus e g in our studies of a type 2 live vaccine virus (Dane *et al*, 1957) we fed a number of individuals with a strain of virus which would not grow in tissue culture and was non paralytogenic for monkeys In the individuals whom we tested we found that a very marked change in the virus had occurred after multiplication in the human gut for the virus which was excreted by these vaccinated individuals was now

able to grow in tissue culture and was paralytogenic for monkeys

It seems to us then, that the virulence of polioviruses may be determined partly by the host One might explain the appearance of epidemics by assuming that this host factor was more operative some years than others I know of no satisfactory explanation for the seasonal incidence of polio other than that some change occurs in the susceptibility of the host and polio virus appears to multiply better in the alimentary tract in the summer than in the winter months I do not imply that climatic changes *per se* are responsible for increased multiplication But something happens in the summer, just as the cyclone or something associated with it precipitated the Mauritius epidemic We are thus accumulating evidence that in Northern Ireland there is no marked difference in the basic strains of poliovirus from non epidemic and epidemic years and that other factors determine whether or not there will be an epidemic

I have already indicated that when they are fed the same quantity and type of virus some families excrete much greater quantities of virus than others and that the incidence of clinical poliomyelitis is greater in families with an index case than in the general population These may be related, in that in hosts in whom the virus multiplies well there is a greater virus population which presents a greater opportunity for a large number of virulent variants to emerge and it may be that in epidemic years there are a greater number of hosts in which this occurs As I said we have no idea why this happens Is something in the host interfering with the multiplication of virus in non epidemic years? Is this absent during epidemics? Does the gut flora play any part—e g by enhancing virus multiplication in epidemic years? Or is the host factor a dietetic one? If we only knew this we could perhaps return epidemiologically to the pre 1890s, with a well adjusted parasite which never produced epidemics of paralytic disease—without the need of vaccination Until recently we tended to think largely in terms of the seed—now we are thinking much more about the soil as far as the outcome of infection with poliovirus is concerned

Effects of Vaccination

Antibody after Salk vaccine

After vaccination with the Salk type of vaccine (which of course contains inactive polioviruses of all three types), antibody develops to each type of virus and appears in the circulation We do not know how durable this antibody will be It is clear (Figure 5) that the level of antibody after primary immunization

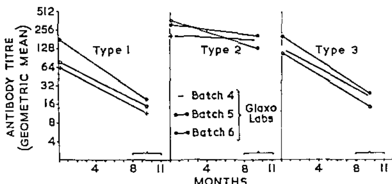


Figure 5 Showing decline in type 1 2 and 3 antibody in children 8–11 months after immunization with Salk vaccine (drawn from Report to M R C 1957a) The response with three different batches of vaccine is shown

with Salk vaccine falls fairly rapidly in the case of the type 1 and 3 components the fall in type 2 antibody is less dramatic There is evidence from American studies that after vaccination the antibody may fall to indetectable levels but Salk (1955 and 1957) has indicated that immunity may last even after cir culating antibody has disappeared below a detectable level and has evoked a theory of immunogenic hyper reactivity I have not the space to discuss his evidence for this theory but he has postulated that once a protective level of antibody has been induced by a sufficient stimulus, even with the disappearance of demonstrable antibody the prevention of paralysis may be mediated through the operation of hyper reactivity Salk has suggested that this hyper reactivity would so condition the body that after ingestion of virus by a natural route a rise in antibody

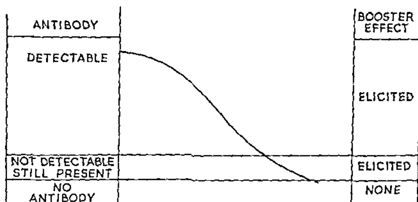


FIGURE 6 Showing theoretical fall in antibody and time when booster effect (hyper reactivity) *may* be elicited

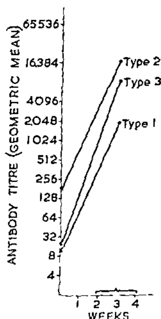


FIGURE 7 Showing response to third shot of vaccine (drawn from Report to M R C 1957a)

would occur in a sufficiently short time to provide adequate antibody protection in the blood to prevent CNS invasion

It seems to us that if hyper reactivity occurs in individuals devoid of antibody, what it may mean is that it occurs in individuals devoid of *demonstrable* antibody One may visualize the fall of antibody as indicated diagramatically in Figure 6 It seems quite possible that a hyper reactive response could occur after antibody had fallen to indetectable levels but was nevertheless present in adequate amounts to cause a booster response to be evoked But it seems doubtful if there will be any hyper reactivity when all antibody has been lost Be that as it may, Salk (1957) has nevertheless advised two doses separated by an interval of 2–6 weeks followed by a third dose not earlier than 7 months later I think this third booster shot is very important

The booster effect of a third shot between 8 and 11 months after primary immunization produces very high levels of antibody as seen from Figure 7 which shows the antibody rise in a group of individuals bled 2–3 weeks after the booster (Report 1957a) These high levels of antibody will fall away also, but probably over a good many years and further shots may be required, for as far as we can gather from North America, information is now being collected to find out when 'fourth shots should be recommended as a universal public health procedure'

In Northern Ireland where we have advised that there should be concentration on vaccination of under 5 year olds (in which age group 80 per cent of paralytic cases occurred in Belfast in 1957) we have also advised that a third shot should be given to those already vaccinated before extending the use of limited vaccine to older age groups Our reason for this is that until we have evidence to the contrary we feel that if the antibody level falls as shown by the Report to the Medical Research Council (1957a) (see Figure 5) and if there is a delay of several years before the third shot is given the children primarily immunized may find themselves in a virgin antibody state (see Figure 6)—again requiring primary immunization This may not occur of course because of the intensive natural immunization which occurs in Northern Ireland which will boost the antibody produced by vaccination

Effect of immunization on the community

What effect then will immunization of a community with Salk vaccine have on the natural history of the virus?

There is a great deal of evidence which indicates that circulating antibody will prevent invasion of the CNS by polio viruses, and the effect of Salk vaccine in preventing paralytic poliomyelitis for the season after vaccination can be seen from the American field studies and those made in the United Kingdom which are summarized in Table 3 from a Report to the Medical Research Council (1957b)

TABLE 3 Showing attack rate of paralytic polio in children who received 2 injections of vaccine (From Report to MRC 1957)

Age group (years)	Paralytic attack rate per 100 000 in	
	Vaccinated	Controls
1½–5½	4 1	20 1
5½–9½	1 3	8 2

Does the presence of antibody induced by Salk vaccine have any influence on alimentary infection and alimentary multiplication of virus? Is Salk vaccination likely to have any effect on the transmission of virus in the community similar to the effect which e g diphtheria immunization has on the spread of diphtheria bacilli? Fox (1957b), from studies in Louisiana, has concluded that the immunity induced by a primary course of Salk vaccine (i e two injections of vaccine) does not influence alimentary infection with poliovirus In another study Paul, Horstmann Melnick Niederman and Deutsch (1957) have compared the occurrence of natural infections in children with Salk vaccine and their non vaccinated siblings The question asked was whether individuals vaccinated with Salk vaccine differ in their reaction to exposure to poliovirus in their homes as compared with other members of the same family Paul and his associates (1957) concluded that there was no difference in the excretion of virus on the part of vaccinees and non vaccinees of comparable age groups The conclusion of these investigators

is not, in my opinion, justified, for in their study they have not recorded either quantitative measurements of the virus excreted nor do they give any information on the duration of excretion nor of the levels of antibody in the vaccinated individuals

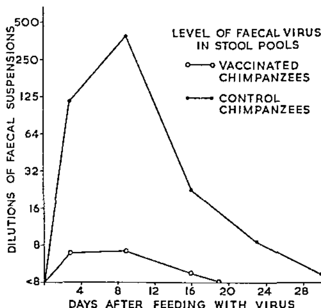


FIGURE 8 Drawn diagrammatically from Howe (1957) showing the difference in faecal excretion of poliovirus in vaccinated and unvaccinated chimpanzees

There may have been very great differences in the quantity and duration of virus excretion in the vaccinated and non vaccinated children whom they studied Let me illustrate this from some experiments on chimpanzees Howe (1957) has shown that after a course of Salk vaccination the quantity of virus excreted by vaccinated chimpanzees was very much less than in control animals The difference in the duration of excretion was not very great, and without quantitative measurements, it would have been concluded that there was no difference in the excretion of virus by the vaccinated and non vaccinated animals Howe has concluded from these experiments that his observations might

be extrapolated to suggest that mass vaccination with Salk vaccine will appreciably affect the epidemiology at least in certain segments of the population by limiting virus spread Before drawing any conclusions, however, on the bearing of these experiments to what happens in humans, we must bear in mind that oropharyngeal virus multiplication in chimps is much greater than in man For this reason the influence of circulating antibody on the multiplication of virus in the alimentary tract may not be the same in the two species Although the available evidence suggests that primary vaccination of humans with American Salk vaccine does not appear to interfere with alimentary multiplication of virus, we have no information as to what influence high levels of Salk induced antibody, such as those produced by booster shots, may have

In the evaluation of the efficiency of vaccines in preventing paralysis in the community it is very important that laboratory studies be made in all virus infections of the CNS Apart from antibody studies, no information is yet available on the effects which immunization is having on the incidence of paralytic poliomyelitis in Great Britain In Northern Ireland we attempt to establish the cause of all infections of the CNS We think that this is important and will be of increasing importance in vaccinated children for there are many viruses which can mimic poliomyelitis It is of interest to note that last year in four individuals who were diagnosed as having paralytic poliomyelitis but from whom no poliovirus was recovered and in whom there was no serological evidence of a recent poliomyelitis infection, we were able to demonstrate serological evidence of infection with a member of the Russian spring summer encephalitis/louping ill group of viruses (Likar and Dane, 1958) Without virological studies these cases would have been undiagnosed Had they occurred in vaccinated individuals they would have been considered as vaccine failures The effect of immunization on the community can only be properly established by the co operation of the clinician the Medical Officer of Health and the virologist, for without the latter it is often quite impossible to make an accurate diagnosis of many infections of the CNS

Effect of Salk vaccination on the natural history

What will be the outcome of Salk vaccination on the natural history of poliomyelitis? There is no doubt that it is effective in reducing the incidence of paralysis (see Table 3). Although the evidence is not yet available it seems to me that it is probable that individuals with high levels of Salk induced antibodies may be poor hosts of poliomyelitis viruses. Is it then possible that as a result of vaccination there will be a greatly decreased dissemination of virus by children? If so, will adults fail to get the repeated natural immunizing infections which may be responsible for maintaining their immunity, and—unless we also repeatedly vaccinate adults and old people—will poliomyelitis find as its hosts the old people in the community. In twenty years time is it possible that we shall be seeing senile and not infantile paralysis? This may not happen of course if adults are also reimmunized, and may also not happen because in general, adults are poor virus transmitters. Time will tell, but we should at least be trying to plan experiments to discover what effect vaccination is likely to have on the natural history of the virus.

Immunity after natural infections

It is of interest at this point to compare the durability of immunity and alimentary resistance to reinfection following a natural infection with that after Salk vaccination. This has of course a considerable bearing on the immunity which may be expected to follow oral administration of live virus vaccines.

Paul, Riordan and Melnick (1951) have presented data from an Esquimaux community which indicated that after natural infections antibody to type 2 virus persisted for at least twenty years and that antibody to types 1 and 3 viruses may persist for thirty or forty years. This study is often quoted to indicate that antibody acquired after infection is durable. It should be noted that the population group studied was a highly susceptible one (Paul *et al.* 1951) and caution must be used in applying this data from an inbred highly susceptible Esquimaux community to all people and to all strains of poliovirus which may differ in their invasiveness and ability to stimulate antibody. We have evidence from studies of feeding live avirulent viruses that

with time the antibody level declines This is in agreement with the findings of Schmidt and Lenette (1957) that antibody declines after *natural* infections They found a four fold or greater drop in neutralizing antibodies against the infecting virus in 33 of 51 paralytic patients between three months and two years after the acute phase of the disease A two fold decline was shown by 12 and only 6 showed no change in titre at the end of two years It may be concluded that we do not yet know how durable is the antibody which develops after a natural infection Certainly there is a fall We do not know whether low levels of antibody persist for life without the booster effect of re-infections

Reinfection

With regard to reinfection of the alimentary tract Fox, Gelfand, Le Blanc and Conwell (1957) have concluded that reinfection appears to be a common event especially in those with low levels of naturally acquired antibody It appears, however, that in individuals undergoing reinfection, excretion of virus occurs only for a relatively brief period The evidence of Fox and his colleagues (1956) also suggests that in naturally immune individuals who have been reinfected the spread of virus is greatly restricted Much of this work is however, difficult to interpret because, as I have said the degree of virus excretion may vary at different times of the year and also as children grow older they tend to excrete less virus than when they are small so there are these additonal factors to consider in assessing what happens in reinfections It is also very difficult to get information on the frequency of reinfection in relation to the level of antibody at the time of reinfection Both Sabin (1957, 1958) and Paul *et al* (1957) have shown that individuals who have developed immunity after feeding with live virus vaccines are at least for a time relatively resistant to reinfection with live virus vaccines as compared with individuals who have not experienced a previous infection

We may summarize the available information as follows If an individual has undergone a natural infection or has been fed with live virus then the alimentary multiplication of virus after

reinfection or refeeding appears to be modified for some time Primary vaccination with American Salk vaccine does not appear to interfere with alimentary multiplication of virus We have, as has been said, no information as to what influence high levels of Salk induced antibody may have on the alimentary multiplication of virus At the present time the data on antibody levels in relation to resistance to alimentary infection are so meagre that it is unwise to postulate a different type of immunity in individuals who have developed antibody as the result of natural infections compared with those who have developed antibody as a result of immunization with Salk vaccine, i e there is no evidence that Salk vaccinated and naturally immunized individuals behave differently as far as the alimentary multiplication of virus is concerned if they are challenged with live virus at the same interval after attaining their maximum antibody titres On the other hand they may differ in their resistance to alimentary reinfection, for even with the same levels of circulating antibody it may be that after a natural infection or feeding of live virus vaccines there is a concentration of antibody in the wall of the gut which may influence the alimentary carriage of virus, and the transmission of virus from person to person

Live virus vaccines

I have already noted that polioviruses immunize many people but usually produce paralysis only occasionally Several investigators have tried to develop strains of live virus which would immunize but never paralyse and this led Koprowski (Koprowski Norton Jervis Nelson Chadwick, Nelsen and Meyer, 1956), Sabin (1958) Paul *et al* (1957) Horstmann (1958) Cox (da Silva McKelvey Prem Bauer Cooney and Johnson 1957), and our own group in Belfast (Dane *et al* 1957 Dick *et al*, 1957 Dick and Dane, 1957) to investigate the use of live avirulent or attenuated strains of polioviruses as oral vaccines I have already indicated from the virus feeding studies which I mentioned how these attenuated strains behave in human beings They behave like the less virulent naturally occurring polioviruses Like naturally occurring strains they can spread

from person to person Now some people do not consider that this spread is important and it has been argued that the spread of attenuated strains in a community will replace the more dangerous paralytic strains The extent of the spread which can occur may be seen (Table 4) from a recent study by da Silva and his co workers (1957) who fed 25 infants in succession with attenuated strains of type 1, 2 and 3 viruses developed by Cox

TABLE 4 Showing contact infections among mothers and siblings of babies fed with types 1 2 and 3 polioviruses (from da Silva *et al*, 1957)

Type of virus	Contact infections (%) among	
	Siblings	Mothers
1	68	8
2	16	0
3	60	44

Not only can these vaccine strains spread from person to person but in all studies which have been done with live virus *vaccines there has been a change of the virulence of the vaccine* viruses during their multiplication in the gut of some individuals It appears, therefore that when these vaccine viruses are excreted they cannot be differentiated from some naturally occurring strains I mentioned our studies of strains of viruses from paralysed children and their asymptomatic contacts infected with presumably the same virus (Table 3) If naturally occurring avirulent strains may become virulent on multiplication in the gut so also may those attenuated viruses used for vaccines We cannot therefore visualize that a virus which is excreted in a form unrecognizable from some wild viruses and can spread readily, is likely to be without danger All the presently available strains of live virus vaccines are in our opinion inacceptable for wide scale use and we do not agree with the recommendations of the World Health Organization expert committee that wide scale trials should be undertaken This does not mean that the future of live attenuated vaccines is hopeless and we are actively investigating this problem

Conclusion

I indicated at the outset that there are a great many unknowns about poliomyelitis, and I have failed to provide complete answers to the questions which I put at the beginning of this lecture What happened in London in 1947? Why was polio myelitis epidemic in Belfast in 1957? Although we have failed to answer those questions I hope that I have shown along what lines Dr Dane and my other colleagues in Belfast and I are thinking More and more we are thinking that the host deter mines the virulence of the virus that this host factor may be more operative at certain times of the year, and that epidemics of paralytic disease may depend more on host factors than has been previously considered It may be that these questions will remain unanswered as paralytic poliomyelitis disappears from the community as a result of vaccination What will happen to the natural history of the virus as a result of vaccination we have yet to discover There is a long way to go in solving these prob lems but the solution will be made on that fringe of science which applies to medicine—on which this series of lectures on the scientific basis of medicine has been set

REFERENCES

Andrewes C H (1940) *Proc roy Soc Med* 33 75

Bradley W H (1950) *Month Bull Minist Hlth Lab Serv* 9 203

Dane D S Dick G W A Connolly J H Fisher O D McKeown Florence (1957) *Brit med J* i 59

Dick G W A and Dane D S (1957) *Brit med J* i 70

Dick G W A Dane D S Fisher O D Connolly J H and McKeown Florence (1957) *Brit med J* i 65

Fox John P (1957a) In *Cellular Biology Nucleic Acids and Viruses* Special publications N Y Acad Sci Vol V 152

Fox J P (1958) *Poliomyelitis Papers and discussions presented at 4th Int Conference* Ed Internat Polio Congress J B Lippincott Co Phil p 136

Fox J P Gelfand H M Le Blanc Dorothy R and Connell D P (1956) *Am J pub Hlth* 46 283

Horstmann Dorothy M (1958) *Poliomyelitis Papers and discussions at 4th Internat Conference* J B Lippincott Co Phil p 152

HORSTMANN, DOROTHY M McCOLLUM R W and MASCOLA ANNE D (1955) *J clin Invest* 34 1573
HOWE, H A (1957) *Am J pub Hlth* 47 871
KOPROWSKI H NORTON T W JERVIS G A NELSON T L CHADWICK D L NELSEN DORIS J and MEYER K F (1956) *J Amer med Ass* 160 954
LIKAR M and DANE D S (1958) *Lancet* i 456
McFARLAN A M DICK G W A and SEDDON H J (1946) *Quart J Med* (N S XV) 59 183
PAFFENBARGER R S JR WILSON V O, BODIAN D and WATT J (1954) *Am J Hyg* 60 63
PAUL J R HORSTMANN DOROTHY M MELNICK, J L NIEDERMAN J C and DEUTSCH, JOYCE (1957) In *Cellular Biology Nucleic Acids and Viruses* Special publications of N Y Acad Sci Vol V 141
PAUL J R RIORDAN, J T and MELNICK J L (1951) *Am J Hyg* 54 275
REPORT TO THE MEDICAL RESEARCH COUNCIL (1957a) *Brit med J* i 1271
REPORT TO THE MEDICAL RESEARCH COUNCIL (1957b) *Brit med J* ii 1207
ROBB A GARDNER (1916) *Recent epidemic outbreaks of acute poliomyelitis* A paper read before the Ulster Med Soc 4 Nov 1915 Belfast Graham and Heslip
SABIN A B (1955) *Brit med J* ii 160
SABIN A B (1957) In *Cellular Biology Nucleic Acids and Viruses* Special publications N Y Acad Sce vol v 113
SABIN, A B (1958) *Poliomyelitis Papers and discussions at 4th Internat Conference* J B Lippincott Co Phil p 124
SALK J E (1955) *Ann N Y Acad of Sci* 61 1023
SALK J E (1957) *Am J pub Hlth* 47 1
DA SILVA M M McKELVEY J L PREM K D, BAUER H COONEY MARION K and JOHNSON EUGENE A (1957) *Univ of Minnesota med Bull* 29 133
SCHMIDT N J and LENETTE E H (1957) *Am J Hyg* 66 119
TURNER T B HOLLANDER D H BUCKLEY S KOKKO, U P and WINSOR C P (1950) *Am J Hyg* 52 323
WORLD HEALTH ORGANISATION (1958) Expert Committee on poliomyelitis Second report W H O Technical report series No 145 W H O Geneva
WICKMAN O I (1913) *Acute poliomyelitis* Nervous and mental disease monograph series No 16 N Y, J Nervous and Mental disease Pub Co

XXII

Potassium Deficiency

P FOURMAN

POTASSIUM it is said, is of the cell and sodium of the sap But the division is not absolute, nor are the differences in the biological functions of these two cations a simple matter of distribution There is in fact some sodium in the cells, and both ions constantly move back and forth across the cell membrane which is permeable to both The great difference in the concentrations of the ions on the two sides of the membrane must be maintained by a process of active transport involving the expenditure of energy, pumping sodium out of the cell and potassium into it Although the entry of potassium into the cell could be the passive result of the extrusion of sodium, the difference in biological behaviour between potassium and rubidium, which are closely related chemically, suggests that the inward transport of potassium is an active process (Relman, 1956 Relman *et al* 1957)

The living cells, by maintaining the difference in the concentrations of ions inside and outside them, play an important part in governing the composition of the extracellular fluid which is spread out as a thin film over their surface (Manery, 1954) The kidneys make their contribution to the composition of the extracellular fluid by virtue of receiving one fifth of the heart s output of blood but the composition of the blood they receive is what the cells have made it Factors such as anoxia or disturbances of acid base balance may diminish the efficiency of the cell pumps and may even permit high extracellular concentrations of potassium in the face of a cellular deficit

Since the ions of sodium and potassium are charged particles they cannot move very far without being either accompanied by

an anion of opposite charge or exchanged for another cation of like charge Changes in the concentration of sodium in the *extracellular fluid* are in general accompanied by corresponding changes in the anions, chloride and bicarbonate, whereas changes in the potassium of the cells are more likely to involve an exchange with sodium or hydrogen ion (Darrow and Heller stein, 1958) *The renal excretion of potassium is by a process of* tubular secretion involving an exchange of potassium with sodium (Berliner, 1954, Mudge, 1954, Howell and Davis, 1954, Koch *et al* 1956, Black *et al*, 1956) In this exchange potassium competes with hydrogen (Berliner *et al* 1951)

Biochemical Role of Potassium

Potassium is a much more interesting ion than sodium The main function of sodium is to give the extracellular fluid an osmotic pressure equal to that of the cellular fluid Inside the cells, potassium is only one of a number of substances organic as well as inorganic, that contribute to the osmotic pressure, and it is more important in other ways

Potassium is essential to the action of certain enzymes, in particular transphosphorylase, which catalyses the transfer of high energy phosphate bonds in the formation of adenosine tri phosphate from adenosine diphosphate The enzymic reactions in which potassium is concerned probably take place in the mitochondria, where the concentration and turnover of potas sium are higher than in the remainder of the cell (Bartley and Davies 1952 Spector, 1953, Stanbury and Mudge, 1953, Mac Farlane and Spencer 1953 Gamble, 1957) In enzyme reactions the action of potassium may be antagonized by sodium

At the surface of the cell potassium has quite different func tions decreasing membrane permeability and increasing neuro muscular irritability These actions are antagonized by calcium ions and either excess of potassium or deficiency of calcium immediately outside nerve fibres can produce tetany

Early Studies of Potassium Deficiency

From these considerations a deficiency of potassium might be expected to produce more complex results than a deficiency of

sodium Yet the clinical effects of potassium deficiency were not studied until after the last war (Darrow, 1950 Elman *et al*, 1952) much later, that is than the effects of sodium deficiency Some earlier experimental studies of potassium deficiency in animals had revealed that the loss of potassium was mainly from the muscles, and that sodium to some extent replaced the potassium in them (Heppel 1939 Muntwyler *et al*, 1950) However the concentration of potassium in the liver the heart and the kidneys remained nearly normal In the brain too the concentration of potassium remains normal in the face of a deficiency (Fourman *et al* 1956) On the other hand, some of these organs the heart and the kidneys are the first to show structural evidence of potassium deficiency (Schrader *et al*, 1937 Follis *et al*, 1942) It was some years before these morphological changes were correctly interpreted in human pathology A distinctive vacuolar nephropathy described with intestinal disease (Jaffe and Sternberg 1920, Kulka *et al* 1950) is now recognized to be a result of potassium deficiency (Perkins *et al* 1950)

Causes of Potassium Depletion

One of the reasons why the clinical problem of potassium deficiency was neglected for so long is that with potassium as with sodium the most important cause of a deficiency is the loss of gastro intestinal secretions, whether by vomiting diarrhoea, or fistulous discharge But, as the data of Lans and his colleagues (1952) in Table 1 show the sodium content of the secretion is 10 or 20 times the potassium content Thus until sodium deficiencies were recognized and corrected patients were apt to die of sodium deficiency before they could suffer a serious depletion of potassium As deficiencies of sodium came to be corrected deficiencies of potassium were revealed Now that deficiencies of potassium are corrected deficiencies of magnesium are beginning to be noted (Hammarsten and Smith, 1957)

Loss of potassium from the kidney is less common and generally more insidious than from the gastro intestinal tract It may be a prominent feature of the Fanconi syndrome (Bickel *et al*, 1952 Milne *et al* 1952) and of renal acidosis

(Brown *et al*, 1944, Albright *et al*, 1946, Foss *et al*, 1956) The loss of potassium cannot be ascribed to the acidosis of these syndromes, since it persists when the acidosis is corrected by alkali (Fourman and McCance, 1955, and unpublished observations)

TABLE 1 Average values and ranges of sodium potassium and chloride ions in gastrointestinal fluids (Lans Stein and Meyer 1952)

	No of specimens	No of patients	Sodium mEq/L	Chloride mEq/L	Potassium mEq/L
Gastric juice (free HCl)	76	26	56 (21–82)	126 (76–157)	12 6 (6 5–26 0)
Gastric juice (no free HCl)	65	19	65 (24–126)	72 (36–122)	11 2 (4 8–25 6)
Bile	48	27	151 (137–181)	103 (94–126)	5 2 (3 0–9 2)
Mixture of gastrointestinal secretions	64	41	113 (46–117)	104 (24–127)	4 6 (3 2–16 1)
Small bowel secretions	12	3	121 (88–146)	98 (91–119)	9 6 (4 8–13 6)
Duodenal fistula	19	2	96 (75–119)	61 (52–82)	8 1 (7 2–13 7)
Ileal fistula	12	3	132 (129–138)	68 (35–76)	6 2 (4 6–9 1)
Cecostomy drainage	17	6	69 (52–74)	38 (26–49)	8 2 (4 6–14 0)

Increased renal loss of potassium was recognized some time ago as a complication of Cushing s syndrome (McQuarrie *et al*, 1937, Willson *et al* 1940) and potassium deficiency accounts for nearly all the manifestations of primary aldosteronism (Conn, 1955, Milne *et al* 1957) The loss of potassium depends on the exchange of potassium for sodium in the renal tubule, and it can be diminished if the amount of sodium available for reabsorption in the distal tubule is reduced by curtailing the dietary intake of sodium (Bartter, 1956) It is worth noting that the effect of adrenal cortical hormone on potassium is not restricted to the kidneys It also increases the loss of potassium

in the sweat, in the saliva, and in the faeces (Figure 1) This may explain why the amounts of potassium lost in the secretions in disease can be greater than would be expected from a knowledge of the potassium content of normal secretions (Nadler, 1953)

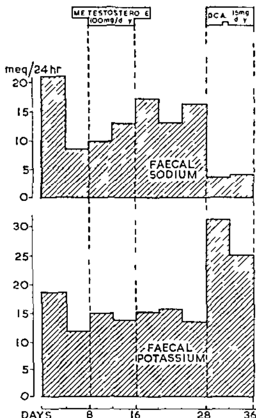


FIGURE 1 Effect of deoxycortone acetate compared with the effect of methyl testosterone on the faecal excretion of sodium and potassium in a patient with Addison s disease not previously treated (Fourman 1952b) Reproduced by permission of the editor of *Clinical Science*

for there is some reason to believe that there is often an increased secretion of cortical hormone in disease (Eliel *et al*, 1950 1952) This may also account for the frequent failure of the kidneys to

conserve potassium in *ill* people (Tarail and Elkinton, 1949) whereas they do conserve it in normal people (Fourman, 1952a)

An alkalosis may increase the renal excretion of potassium (Franglen *et al*, 1953) *This is to be explained by the competition of* K^+ *and* H^+ *ions for exchange with* Na^+ *ions in the renal tubule*, in an alkalosis the reabsorption of H^+ ions is increased, and that of K^+ ions diminished Alkalosis is sometimes responsible for the potassium depletion associated with pyloric stenosis (Davies *et al*, 1956)

Potassium deficiency is now well known to complicate diabetic coma, and there are a number of reasons for it (Mach, 1954) Anorexia curtails the intake of potassium and the losses are increased by vomiting and perhaps by diarrhoea The *glycosuria and the acidosis produce an osmotic diuresis* The adrenal secretion is increased Insulin augments the need for potassium, by causing glycogen to be laid down, and with it water and the other constituents of intracellular fluid (Willebrands *et al* 1952)

A loss of potassium from the body does not necessarily signify a deficit, since potassium must be lost together with other constituents of protoplasm in wasting diseases, this clearly does not entail a fall in the concentration of potassium in the tissues It should be pointed out however that the amounts of potassium *involved in the growth and destruction of protein tissues are* relatively small, less than 3 mEq per gram of nitrogen

Experimental Deficiencies in Man

In 1950 we undertook experiments to determine how much potassium could be lost from the body before clinical effects became obvious and to study those effects in people who were otherwise healthy

The first difficulty was that all normal diets contain potassium, and even the poorest foods contain a lot of it The best we could achieve with a normal intake of protein, was a diet containing 30 mEq per day of potassium, because this intake exceeded the faecal and urinary losses, it could not lead to a deficiency At that time the use of exchange resins was being explored for removing sodium from the body in oedematous

patients and we decided to use them to remove potassium (Fourman, 1953) We gave resin by mouth either in the hydrogen form or the ammonium form, H^+ and NH_4^+ were exchanged for K^+, the former being absorbed and the latter

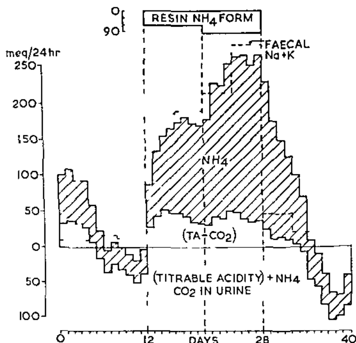


FIGURE 2 The urinary titratable acidity and ammonium and the faecal sodium and potassium in experimental potassium deficiency induced with an exchange resin Titratable acidity (clear area) is plotted from the zero line Negative values indicate that the urine was alkaline Ammonium (hatched area) is plotted up from the values for the titratable acidity Hence the sum of the two representing hydrogen ion excretion is measured from the zero line The sum of faecal sodium and potassium is shown by an interrupted line Reproduced by permission of the editor of *Clinical Science*

excreted with the resin in the faeces In the body ammonium ions are equivalent to hydrogen ions as the ammonium ion may be considered as a molecule of ammonia and a hydrogen ion and the ammonia is metabolized to urea

Figure 2 shows the general design of the experiments and the

fate of the hydrogen ion which entered the body in exchange for the potassium and sodium taken up by the resin It must be emphasized that the resin did not produce sodium depletion in these experiments, but it did prevent the absorption of the dietary sodium

After a preliminary period of control observations on the experimental diet we gave the resin for 12 or 16 days, in a dose of 60 and then 90 g daily The excretion of titratable acid increased from negative values in the control period, corresponding to an alkaline urine, to about 40 mEq daily The excretion of ammonium increased to 150 and even 200 mEq daily The titratable acidity and ammonium together represented an excretion of H^+ ion almost as large as the increased loss of sodium and potassium in the faeces and therefore almost as large as the amount of H^+ ion given off by the resin, but the excretion was not large enough to prevent an acidosis and a fall in the plasma bicarbonate In the period after the administration of resin the subjects continued to take the low potassium diet and therefore did not restore their deficit of potassium But they now absorbed the sodium in their diet, it was being given in the form of organic salts of sodium, such as the citrate or the tartrate, and their acidosis was rapidly corrected

Symptoms and Signs

The deficits of potassium in five experiments ranged from 200 to 800 mEq The milder deficits produced no definite symptoms, beyond anorexia and constipation One of the subjects at the end of his experiment actually went climbing while he still had a deficit of some 500 mEq of potassium, he did not know this at the time In two of the experiments the deficits were severe and symptoms were prominent (Fourman, 1954a) The subjects were weak and had no desire for food, they became very constipated Their skin became sallow and darker than normal There was no fall in blood pressure, although this can be a serious feature of clinical deficiencies The electrocardiographic changes were slight only one subject aged 54 and rather older than the others had inverted T waves His deficit was a mild one and he had minimal symptoms In the other subjects the

only change was the appearance of U waves The electro cardiogram cannot in fact be relied upon to reveal a deficit of potassium either outside or inside the cells (Schwartz *et al* 1954)

Perhaps the most striking symptoms in our subjects were mental, they could not concentrate they lacked judgement and they were extremely bad tempered One subject, W , took to her bed and for several days was almost oblivious to her surroundings though single minded in wanting to continue with her experiment There were three symptoms which were at that time quite unexpected—thirst tetany and oedema They were encountered with mild as well as severe deficits but not in all the experiments

Thirst

Thirst was very prominent in one of the experiments where the subject drank 8 litres of water a day without, however, obtaining any relief Several interpretations are possible One we favour is that deficiency of potassium can act as a direct stimulus to the thirst centre in the hypothalamus In view of the physiological antagonism of potassium and calcium the fact that an excess of calcium can stimulate thirst (Fourman and Leeson, 1959) makes the hypothesis an attractive one, but certain alternatives need to be considered Acidosis was a feature of our experiments and it can stimulate thirst In potassium deficiency the renal tubules fail to conserve water (Brokaw, 1953 Dustan *et al* , 1956) and the resulting polyuria might be held to account for thirst by producing dehydration There was, however, no evidence of dehydration in our experiments and recently Hollander and his colleagues (1957) have observed that rats made deficient in potassium increased their intake of water before there was any evidence of their kidneys failing to conserve it For this reason it seems likely that in the syndrome of diabetes insipidus in potassium deficiency (Ferrebee *et al* 1941 Smith and Lasater 1950) polydipsia can be the cause of the polyuria The polydipsia induced with deoxycortone (Ragan *et al* , 1940) may well have been an effect of the potassium deficiency which the hormone produces

Tetany

Tetany appeared during the period of recovery from acidosis in two of the experiments (Fourman, 1954b) We also observed it in a patient who was being treated for potassium deficiency resulting from renal acidosis (Fourman and McCance, 1955), and we have encountered the symptom in two more patients, one with renal acidosis and another with the adult form of the Fanconi syndrome The symptom is surprising tetany is ordinarily associated with a fall in the ionized calcium of the extracellular fluid, and on the basis of the physiological antagonism of potassium and calcium one could expect potassium deficiency to protect against tetany Tetany in potassium deficiency must, of course, often be the result of an accompanying alkalosis (Darrow *et al*, 1948), but an alkalosis did not account for it in our examples We thought that these people who had been deficient in potassium were responding to small amounts of potassium as normal people would respond to an excess (Bedford, 1954) There is some indication that this abnormal response is associated with an abnormally high cell content of sodium (Fourman and McCance, 1955)

Oedema

Oedema appeared unexpectedly in one of our first experiments after the administration of resin had stopped and sodium was being absorbed We have since been able to reproduce the oedema experimentally (Fourman and Hervey, 1955) and it has been reported in clinical states of potassium deficiency It is the result of an increased tubular reasborption of sodium, but there is not necessarily any increase in the output of aldosterone (Vernet *et al*, 1956) It responds to the administration of potassium, but not before the whole of the deficit has been restored Its significance still poses an intriguing problem

Paralysis

A description of the symptoms of potassium deficiency must include paralysis of the voluntary muscles although there was no sign of paralysis in our experiments The paralysis resembles that of familial periodic paralysis (McArdle 1956) with which

it must often have been confused (Evans and Milne, 1954) In familial periodic paralysis the attacks are usually associated with a fall in the plasma concentration of potassium, though not with any loss of potassium from the body, the potassium moves into the muscle cells (Zierler and Andres 1957) It should be noted that periodic paralysis is not always associated with a fall in the plasma potassium (Tyler *et al*, 1951) and that an abnormal rise in the plasma potassium can also produce paralysis, for example in renal failure (Bull *et al*, 1953) A loss of potassium from the body rarely produces paralysis, except in the slowly developing deficiencies from renal losses It is still not known what determines whether potassium deficiency will lead to paralysis The ionic shifts associated with the transmission of nerve impulses and the excitation of muscle involve only minute amounts of charged particles and the problem of paralysis is unlikely to be solved by the relatively crude methods of balance studies and tissue analyses Denny Brown (1953) has reviewed the neurophysiological aspects from the clinical stand point Offerijns (1955) has investigated the particular problem of paralysis precipitated by the administration of insulin in diabetic coma He studied the contractions of the muscle of the diaphragm removed from rats which had previously been depleted of potassium He found that with various combinations of extracellular and intracellular deficits of potassium the diaphragm went on contracting quite normally but as soon as he added insulin to the fluid bathing the deficient diaphragm it stopped contracting

CHEMICAL EFFECTS

The deficits which were obtained in our experiments must be considered in relation to the amount of potassium there is normally in the body Few bodies have been analysed Widdowson and his co workers (1951) in Cambridge analysed four corpses one of them dead from drowning the others by disease Forbes and Lewis (1956) analysed two corpses From such data it appears that the body contains about 67 mEq of potassium per kg of fat free weight A man weighing 70 kg one fifth of it fat, would have a total potassium content of 3700 mEq This may be

compared with a content of some 4500 mEq of sodium and 2000 mEq of magnesium

There are more data for the amount of potassium in the body that will exchange with a tracer dose of radioactive potassium (Corsa *et al*, 1950, Aikawa *et al*, 1952 Ikkos *et al*, 1955, Muldowney *et al*, 1957), the amount is about 80 per cent of that found by analysis, because part of the potassium in the body does not exchange rapidly Some of the latter, about a tenth of the total, is in bone (Bergstrom, 1952), another tenth seems to be associated with the cell mitochondria (Holland and Auditore, 1955) The normal range for the exchangeable potassium is wide (Muldowney *et al*, 1957) and for this reason it will not serve in the individual patient to detect a deficit of potassium unless it be a very large one However, the method obviously provides more information than can be had from an analysis of the plasma which represents only the extracellular fluid The potassium in the extracellular fluid is less than 2 per cent of the total

In the early experimental deficiencies in animals it was found that most of the potassium was lost from muscles These normally contain 73 per cent of the total potassium in the body, and the analysis of a sample of muscle might provide the easiest way of getting a reasonably accurate measure of a deficit Some normal values from the literature are brought together in Table 2 They reveal considerable variations, partly attributable

TABLE 2 The amounts of Cl Na and K in human muscle

Author and number of data	Water per cent	M Eq/kg fat free tissue Cl	N	K
Talso *et al* 1953 (16)	77 6 ± 0 6	19 1 ± 3 9	33 7 ± 6 4	94 0 ± 5 9
Wilson 1955 (12)	77 5 ± 0 7	25 6 ± 5 1	40 6 ± 6 0	92 3 ± 7 6
Barnes *et al* 1957 (10)	80 3 ± 1 6	23 1 ± 6 5	43 6 ± 11	91 3 ± 8 3

to differences in the amount of connective tissue (Holliday *et al* 1957) Nevertheless there is much to be said for extending the use of this method of investigation

Mudge and Vislocky (1949) analysed the muscles of a man with an inoperable carcinoma of the duodenum who died without having his deficiency of potassium corrected The potassium

content of the muscle fell progressively from the normal value of 90 mEq per kg to 81, 66 and finally at death to 51 mEq per kg We have analysed the muscle of a woman who died with potassium deficiency, *the result of diabetic coma and its potassium* content was 44 mEq per kg or about half the normal Heppel (1939) had found that rats died when their muscle potassium fell to half the normal In a man weighing 70 kg this would represent a loss of about 1400 mEq of potassium, that is 36 per cent of the total and 45 per cent of the exchangeable potassium Our experiments did not go as far as that in different experiments the losses corresponded to between 15 and 29 per cent of the exchangeable potassium

These deficits produced a fall in plasma potassium concentration, to 2 9 mEq per litre This did not seem very striking to us at the time and it was one reason why we went on with the experiments as long as we did In fact the plasma potassium should be considered in relation to the acid base balance, and our experiments produced an acidosis An acidosis hinders the transport of potassium into the cells and a low plasma potassium in the presence of an acidosis indicates a serious depletion (Burnell *et al*, 1956, Burnell and Scribner, 1957) This is exemplified in the case of potassium deficiency of diabetic coma, when the plasma potassium may be normal in spite of severe potassium deficiency, As the acidosis is corrected potassium enters the cells and the plasma level falls abruptly although there is at this stage no further loss of potassium from the body (Atchley *et al* 1933, Willebrands *et al* 1952)

Two more changes in the composition of the plasma in our experiments may be noted One is that the plasma sodium concentration was raised, and if as may be assumed the osmotic pressure of the cells is the same as that of the extracellular fluid the osmotic pressure of the cells must have been high in spite of the loss of potassium from them The other is that the plasma calcium concentration was diminished and presumably as a result of this the urinary excretion of calcium was extremely small Hypocalcaemia has several times been noted in clinical states of potassium deficiency (Fourman 1954a, Surawicz *et al* 1957) Finburg (1957) investigating hypocalcaemia associated

with hypernatraemia, found that it was associated with a fall in the content of potassium in the carcass The fall in plasma calcium in the experimental and clinical deficiencies in human beings is too small to account for tetany, but it has an interesting theoretical implication since the parathyroid secretion normally prevents any fall in plasma calcium concentration by releasing calcium from bone, a deficiency of potassium must in some way interfere with the liberation of parathyroid hormone or with its action

Changes in Cell Composition

A loss of potassium from the cells must be accompanied either by gain of another cation or by a corresponding change in the anions of the cell We did not take muscle biopsies in our experiments so that the changes in cell composition could only be inferred from the results of balance studies Although a cellular gain of sodium has often been demonstrated in potassium deficiency, the amount of sodium in the body did not change in our experiments, and there was no evidence of a gain of sodium in the cells to replace the potassium lost from them The main anions in the cells are organic compounds of phosphorus and proteins The measured losses of phosphorus were small The direct analysis of muscle from potassium deficient animals has shown that there is an intracellular acidosis (Gardner *et al*, 1952) and hydrogen ions to some extent replace the lost potassium, in other respects the inorganic constituents of the cell may not undergo any major changes though the quantity of sodium inside the cells may increase if sodium is provided in the diet (Cotlove *et al*, 1951) Recently Eckel and Norris (1955) found that the cell content of the basic amino acid lysine increased

The Alkalosis of Potassium Deficiency

An intriguing aspect of potassium deficiency which aroused the curiosity of investigators was that the patients often had an extracellular alkalosis (Darrow, 1950) Our experiments could not solve this problem since hydrogen ion was entering the body in place of the potassium withdrawn from it Black and Milne (1952) in Manchester, took the next step of producing a

potassium deficiency without this complication, by giving a diet of milk which had been passed over a column of resin in the sodium form This type of experiment could not easily produce a severe deficit and it was associated with a large intake of sodium, some 300 mEq daily It also entailed a large intake of phosphate, two or three times the normal but the intake of calcium was low, because the resin column adsorbed the calcium as well as the potassium from the milk Under these conditions large amounts of phosphate were absorbed The experiments produced only a small deficit of potassium but a very definite alkalosis as measured in the plasma that is the concentration of hydrogen ion in the extracellular fluid was reduced The hydrogen ion had not been excreted by the kidney, since the urine had in fact become more alkaline Hydrogen ion had therefore presumably entered the cells, where it replaced some of the potassium lost from them

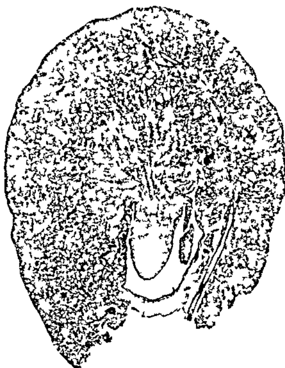
These experiments in man provided confirmation for the hypothesis of Cooke *et al* (1952) based on experiments in rats, that the alkalosis of potassium deficiency was extracellular and the result of a movement of hydrogen ions from the extra cellular fluid to the cells Orloff *et al* (1953) provided further evidence that the alkalosis in the extracellular fluid was not necessarily the result of excretion of H ion by the kidney because, in animals that had had their kidneys removed, they were able to correct the alkalosis of potassium deficiency with potassium chloride a neutral salt Subsequent investigators who have tried to reproduce in man the alkalosis of potassium deficiency have often not been successful (Blahd and Bassett 1953), even when they gave as much sodium as did Black and Milne (Squires and Huth 1955) In rats Seldin and his associates (1956) produced the alkalosis most easily if the intake of phosphate was high and this may have been an important factor in the Manchester experiments It merits further study

THE ROLE OF THE KIDNEY

A shift of hydrogen ions from the extracellular fluid to the cells does not alone explain the extracellular alkalosis because one would normally expect the kidney then to correct it by excreting

bicarbonate In a potassium deficiency the renal cells, like the other cells of the body, are more acid than normal (Anderson and Mudge, 1955), and this may be why they continue to re absorb bicarbonate ion in spite of the extracellular alkalosis At all events the ability to excrete bicarbonate ion is reduced in a potassium deficiency (Cooke *et al*, 1954, Roberts *et al*, 1955) We gave sodium bicarbonate, 300 mEq daily to a patient with a moderate deficit of 200 mEq of potassium (FitzGerald and Fourman, 1955) At the end of three days her plasma bicarbonate had risen to 39 mEq per litre and she had tetany She had retained 780 mEq of sodium and 3 l of water We then gave her potassium bicarbonate as well as the sodium bicarbonate, and her kidneys promptly corrected the alkalosis by excreting sodium and bicarbonate ion It may be recalled that the alkalosis of pyloric stenosis may not respond to treat ment unless any underlying potassium deficiency is first cor rected (Burnett *et al*, 1950, Black and Jepson, 1954)

Potassium deficiency interferes with some of the other functions of the renal tubules We have mentioned the dimi nished reabsorption of water (Dustan *et al*, 1956, Hollander *et al*, 1957), and it is of interest that a similar disturbance can arise with calcium excess (Cohen *et al*, 1957) Milne (1956) has discussed at length the renal responses to acidosis in potassium deficiency, emphasizing that the pH of the urine does not diminish in the normal way In spite of this, ammonia is pro duced in normal amounts, as we have noted Schwarz and Rel man (1953), in a classic study of potassium deficiency from the abuse of laxatives, noted also a diminished tubular transport of para amino hippuric acid These disturbances are probably related to the structural lesions which were demonstrated long ago in the proximal tubules and the collecting tubules in potassium deficiency They have recently been investigated again by a number of new histological techniques (Schwartz, 1955, Oliver *et al* 1957, Craig and Schwartz, 1957 Pearse and MacPherson, 1958) The alterations in both structure and function seem generally to be reversible, we have recently been able to demonstrate normal clearances of inulin and of para amino hippuric acid in one man who was twice the subject of



(a)



(b)

FIG 3 *(a)* Enlarged kidney with dilatation of tubules from a rat on normal diet for seven months after an initial period of potassium deficient diet compared with *(b)* normal sized kidney of control rat at the

our early experiments and who sustained one of the largest depletions

There are however examples where the kidneys did not become normal after the correction of a potassium deficiency (Chalmers *et al* 1956, de Graeff 1958) We have been able to produce in rats made potassium deficient for only a few weeks permanent renal damage with uraemia and cardiac hypertrophy (Plate XXXIII, Figure 3*a* *b*, Fourman *et al*, 1956) The reason Milne and his associates (1957) were unable to reproduce this finding was probably that they used younger rats (Kennedy, 1958)

The ageing process is partly a progressive failure of adaptation and homoiostasis (Comfort, 1957) and one may postulate that the ability of the organism to adapt to a deficiency of potassium, and indeed any other form of stress, diminishes with age On the whole, however, it is remarkable how well an animal can withstand a large loss of an intracellular element on which all life and many enzyme systems depend The explanation for the relatively slight effects of a moderate loss of potassium may be that it is not at first lost from the most important organs or from the most important parts of the cell Only when certain tissues, like the heart the kidney and the brain or certain components of the cell like the mitochondria, fail to maintain their potassium content does the effect of a potassium deficiency become serious In young and healthy people this may happen only with very large deficits but it is possible that smaller deficits carry a greater risk whenever there is any interference with the oxidative processes of the cell in certain diseases, and in old age

REFERENCES

AIKAWA J K HARRELL G T and EISENBERG B (1952) *J clin Invest* 31 367

ALBRIGHT F BURNETT C H PARSON W REIFENSTEIN E C and ROOS A (1946) *Medicine (Baltimore)* 25 397

ANDERSON H M and MUDGE G H (1955) *J clin Invest* 34 1691

ATCHLEY D W LOEB R F RICHARDS D W BENEDICT E M and DRISCOLL M E (1933) *J clin Invest* **12** 297
BARNES, B A. GORDON E B COPE O (1957) *J clin Invest* **36** 1239
BARTLEY, W and DAVIES, R E (1952) *Biochem J* **52** 20
BARTTER F C (1956) *Metabolism* **5** 369
BEDFORD P D (1954) *Lancet* ii 268
BERGSTROM W H (1952) *J clin Invest* **31** 617
BERLINER R W (1954) *Ann Rev Physiol* **16** 269
BERLINER R W KENNEDY T J and ORLOFF J (1951) *Amer J Med* **11** 274
BICKEL H SMALLWOOD W C SMELLIE J M and HICKMANS E M (1952) *Acta paediat (Uppsala)* **42** Supp 90 27
BLACK D A K DAVIES, H E F EMERY E W and WADE E G (1956) *Clin Sci* **15**, 277
BLACK D A K and JEPSON, R P (1954) *Quart J Med* **23** 367
BLACK D A K and MILNE M D (1952) *Clin Sci* **11** 397
BLAHD W H and BASSETT S H (1953) *Metabolism* **2** 218
BROKAW A (1953) *Amer J Physiol* **172** 333
BROWN M R CURRENS J H and MARCHAND J F (1944) *J Amer med Ass* **124** 545
BULL G M CARTER A B and LOWE K G (1953) *Lancet* ii 60
BURNELL J M and SCRIBNER B H (1957) *J Amer med Ass* **164** 959
BURNELL J M VILLAMI M F UYENO B T and SCRIBNER B H (1956) *J clin Invest* **35** 935
BURNETT C H BURROWS B A COMMONS, R R and TOWERY, B T (1950) *J clin Invest* **29** 175
CHALMERS T M FITZGERALD M G JAMES A H and SCARBOROUGH H (1956) *Lancet* i 127
COHEN S I FITZGERALD M G FOURMAN P GRIFFITHS W J and DE WARDENER H E (1957) *Quart J Med* **26** 4 3
COMFORT A (1957) *Symp Inst Biol* **6** 27
CONN J W (1955) *J Lab clin Med* **45** 3
COOKE R E SEGAR W E CHEEK D B COVILLE F E and DARROW D C (1952) *J clin Invest* **31** 798
COOKE R E SEGAR W E REED C ETZWILER D D VITA M BRUSILOW S and DARROW D C (1954) *Amer J Med* **17** 180
CORSA L JR OLNEY J M STEENBURG R W BALL M R and MOORE F D (1950) *J clin Invest* **29** 1280
COTLOVE E HOLLIDAY M A SCHWARTZ R and WALLACE W M (1951) *Amer J Physiol* **167** 665
CRAIG J M and SCHWARTZ R (1957) *Arch Path* **64** 245
DARROW, D C (1950) *New Engl J Med* **242** 978 1014
DARROW D C and HELLERSTEIN S (1958) *Physiol Rev* **38** 114
DARROW D C SCHWARTZ R. IANNUCCI J F and COVILLE F (1948) *J clin Invest* **27** 198

Davies H E F Jepson R P and Black D A K (1956) *Clin Sci* **15** 61
de Craeff F (1958) Communication to the Renal Association London
Denny Brown D (1953) *Amer J Med* **15** 368
Dustan H P Corcoran A C and Page I H (1956) *J clin Invest* **35** 1357
Eckel R E and Norris J E (1955) *J clin Invest* **34** 931 (abstract)
Elifl L P Pearson O H and Rawson R W (1950) *New Engl J Med* **243** 471 518
Elifl L P Pearson O H and White F C (1952) *J clin Invest* **31** 419
Elman R Schatz B A Keating R E and Weichselbaum T E (1952) *Ann Surg* **136** 111
Evans B M and Milne M D (1954) *Brit med J* ii 1067
Ferrebee J W Parker D Carnes W H Gerity M K Atchley D W and Loeb R F (1941) *Amer J Physiol* **135** 230
Finburg L (1957) *J clin Invest* **36** 434
FitzGerald M G and Fourman P (1955) *Lancet* ii 848
Follis R H Jr Orent Keiles E and McCollum E V (1942) *Amer J Path* **18** 29
Forbes G B and Lewis A M (1956) *J clin Invest* **35** 596
Fo s G L Perry C B and Wood F J Y (1956) *Quart J Med* **25** 185
Fourman P (1952a) *Lancet* i 1042
Fourman P (1952b) *Clin Sci* **11** 387
Fourman P (1953) *Brit med J* i 544
Fourman P (1954a) *Clin Sci* **13** 93
Fourman P (1954b) *Lancet* ii 525
Fourman P and Hervey G R (1955) *Clin Sci* **14** 75
Fourman P and Leeson P M (1959) *Lancet* in press
Fourman P and McCance R A (1955) *Lancet* i 329
Fourman P McCance R A and Parker R A (1956) *Brit J exp Path* **37** 40
Franglen G T McGarry E and Spencer A G (1953) *J Physiol* **121** 35
Gamble J L (1957) *J biol Chem* **228** 955
Gardner L I MacLachlan E A and Berman H (1952) *J gen Physiol* **36** 153
Hammarsten J F and Smith W O (1957) *New Engl J Med* **256** 897
Heppel L A (1939) *Amer J Physiol* **127** 385
Holland W C and Auditore G V (1955) *Amer J Physiol* **183** 309
Hollander W Jr Winters R W Williams T F Bradley J Oliver J and Welt L G (1957) *Amer J Physiol* **189** 557
Holliday M A Segar W F Lukenbill A Valencia R M and Durell A M (1957) *Proc Soc exp Biol* **95** 786
Howell D S and Davis J O (1954) *Amer J Physiol* **179** 359

IKKOS D, LJUNGGREN H LUFT, R and SJOGREN B (1955) *Metabolism* 4 231

JAFFÉ R H and STERNBERG H (1920) *Arch path Anat* 227, 313

KENNEDY G C (1958) *Ciba Foundation Colloquium on Water and Electrolyte Metabolism in relation to Age and Sex* Churchill London

KOCH A R, BRAZEAU P and GILMAN A (1956) *Amer J Physiol* 186 350

KULKA J P PEARSON C M and ROBBINS S L (1950) *Amer J Path* 26, 349

LANS H S STEIN I F and MEYER, K A (1952) *Surg Gynec Obstet* 95 321

MCARDLE, B (1956) *Brit med Bull* 12 226

MACFARLANE M G and SPENCER, A G (1953) *Biochem J* 54 569

MCQUARRIE, I, JOHNSON R M and ZIEGLER, M R (1937) *Endocrinology*, 1 762

MACH R S (1954) in *Physiopathologie du Potassium* Paris

MANERY J F (1954) *Physiol Rev* 34 334

MILNE M D (1956) *Lectures on the Scientific Basis of Medicine* vol v 1955-6 p 404 Athlone Press London

MILNE M D, MUEHRCKE R C and AIRD I (1957) *Quart J Med* 26, 317

MILNE, M D MUEHRCKE R C and HEARD B E (1957) *Brit med Bull* 13 15

MILNE M D STANBURY, S W and THOMPSON A. E (1952) *Quart J Med* 21 61

MUDGE G H and VISLOCKY (1949) *J clin Invest* 28, 489

MUDGE G H (1954) *Ion Transport across Membranes* Acad Press New York 1954

MULDOWNEY F B CROOKS J and BLUHM M M (1957) *J clin Invest* 36 1375

MUNTWYLER E GRIFFIN G E SAMUELSEN G S and GRIFFITH L G (1950) *J biol Chem* 185 525

NADLER C S (1953) *Amer J med Sci* 226 88

OFFERIJNS F G J (1955) *Over het verband tussen Kaliumdeficiente spierparalyse en insuline* Amsterdam

OLIVER J MACDOWDE M WELT L G HOLLIDAY M A HOLLANDER W WINTERS R W WILLIAMS T F and SEGAR W E (1957) *J exp Med* 106 563

ORLOFF J KENNEDY T J JR and BERLINER R. W (1953) *J clin Invest* 32 538

PEARSE A G E and MACPHERSON C R (1958) *J Path Bact* 75 69

PERKINS J G PETERSEN A B and RILEY J A (1950) *Amer J Med* 8, 115

RAGAN C FERREBEE J W PHYFE P ATCHLEY D W and LOEB R F (1940) *Amer J Physiol* 131 73

RELMAN A S (1956) *Yale J Biol Med* **29** 248

RELMAN A S LARUBIE A. T BURROWS B A and ROY A M (1957) *J clin Invest* **36** 1249

RELMAN A S and SCHWARTZ W B (1956) *New Engl J Med* **255** 195

ROBERTS K E RANDALL H T SANDERS H L and HOOD M (1955) *J clin Invest* **34** 666

SCHRADER G A PRICKETT C O and SALMON W P (1937) *J Nutr* **14** 85

SCHWARTZ W B (1955) *New Engl J Med* **253** 601

SCHWARTZ W B LEVINE H D and RELMAN A S (1954) *Amer J Med* **16** 395

SCHWARTZ W B and RELMAN A. S (1953) *J clin Invest* **32** 258

SELDIN D W WELT L G and CORT J H (1956) *Yale J Biol Med* **29** 2 9

SMITH S G and LASATER T E (1950) *Proc Soc exper Biol Med* **74** 427

SPECTOR W G (1953) *Proc roy Soc B* **141** 268

SQUIRES R D and HUTH E J (1955) *Clin Res Proc* **3** 127

STANBURY S W and MUDGE G H (1953) *Proc Soc exp Biol N Y* **82** 675

SURAWICZ B BRAUN H A CRUM W B KEMP R L WAGNER S and BELLET S (1957) *Amer J med Sci* **233** 603

TALSO P J SPAFFORD N and BLAW M (1953) *J Lab clin Med* **41** 281

TARAIL R and ELKINTON J R (1949) *J clin Invest* **28** 99

TYLER F H STEPHENS F E GUNN F D and PERKHOFF G T (1951) *J clin Invest* **30** 492

VERNET A DUCKERT A. and MULLER A F (1956) *Helv med acta* **23** 490

WIDDOWSON E M MCCANCE, R A and SPRAY C M (1951) *Clin Sci* **10** 113

WILLEBRANDS A F GROEN J and FRENKEL M (195) *Acta med scand* **141** 331

WILLSON D M POWER M H and KEPLER E J (1940) *J clin Invest* **19** 701

WILSON A O (1955) *Brit J Surg* **43** 71

ZIERLER K L and ANDRES R (1957) *J clin Invest* **36** 730

XXIII

The Study of the Circulation by Dye Dilution Curves

J P SHILLINGFORD

STEWART in 1894 first showed that it was possible to estimate the cardiac output by injecting an indicator substance into the venous, and sampling it from the arterial circulation Hamilton Moore, Kinsman and Spurling (1932) demonstrated its application in man and further showed that an estimation of the volume of blood through which the indicator had passed could be obtained More recently the principle has been used to define the position and size of intracardiac shunts and to estimate valvular incompetence The basic principles underlying this technique and its application to the study of the circulation *will be outlined but space does not allow the more detailed* mathematical considerations to be included

The Basic Principle Underlying an Indicator Dilution Curve

Consider fluid passing from left to right through a volume represented by a glass sphere (Figure 1) If an indicator substance such as Indian ink is injected at A the particles will be spread out in their passage through the fluid This spread may be recorded as a time concentration curve as it passes point B The parameters of this curve, in the absence of a shunt or valvular incompetence, are, to a large extent determined by the speed of flow of the fluid and the volume through which it passes If the speed of flow is increased the particles of indicator will reach the sampling point faster and reduce the appearance

time, they will also pass the sampling site more quickly with a decrease in the spread of the curve An increase in volume causes the particles to traverse more fluid and lengthens the appearance time, their dispersion is greater with an increase in the spread of the curve (Figure 2) It is on this basic principle that the study of the circulation by indicator dilution curves is based, but before going on to this in more detail I should first like to discuss some of the methods used for recording the curves

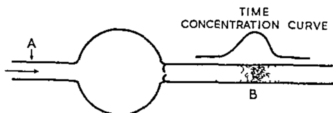


FIGURE 1 The basis of the time concentration curve If a small amount of indicator is rapidly injected at point A the particles will be spread out in their passage through the fluid in the tubes and sphere and may be represented as a time-concentration curve at point B

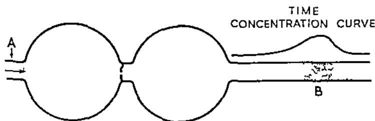


FIGURE 2 The effect of an increase in volume through which indicator passes on the time-concentration curve The particles are more spread out and the resultant curve is widened with a lower peak concentration when compared with Figure 1

METHODS OF RECORDING INDICATOR DILUTION CURVES

Many indicators have been used by various workers in the study of the circulation in man An ideal indicator should meet the following requirements

1 It should be harmless when injected intravenously and cause no discomfort

2 The amount injected should be small in bulk

3 The indicator must remain in the blood stream and not be lost in the tissues or changed in chemical composition during its passage through the body

4 It must be easily sampled and measured by direct or indirect methods

Hering in 1829 injected potassium ferrocyanide as an indicator to estimate the circulation time of the blood Stewart (1897) determined the time concentration curve of salt solution passing through an artery by the change in its electrical conductivity Other chemicals used included thiocyanates and iodides With the development of colorimetry attention was turned to the use of dyes such as tetraiodophenolphthalein and brilliant vital red More recently T 1824 (Evans blue) has become established as a satisfactory dye for obtaining dye dilution curves The loss of this dye from the circulation is negligible over the time needed to calibrate the curve, it appears to be harmless and its concentration is easily measured in the plasma Its absorption spectrum (640 millimicrons), however, is in the region of that of reduced haemoglobin, it is not, therefore, satisfactory in those patients with congenital heart disease and a changing blood oxygen saturation, where continuous photoelectric recording is desired To overcome this Fox and Wood (1958) have introduced a green dye with a spectrum absorption in the region of the wavelength (800 millimicrons) at which the absorption by oxy and reduced haemoglobin are the same At present it is under trial, but preliminary reports are promising

Radioisotopes such as radioactive iodinated human serum albumen, inorganic radioactive iodide and radioactive sodium, have all been used as tracers to produce indicator dilution curves Unfortunately the amount of the substance needed to produce time concentration curves on the radioactivity recorder placed over a peripheral vessel tends to exceed the safety limit and precludes multiple injections Many early workers used the intermittent sampling technique in which blood was allowed to flow through an indwelling arterial needle into a series of tubes which collected the blood at timed intervals of one or two seconds The development of the photoelectric cell and suitable

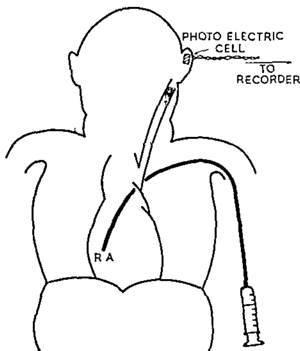


FIGURE 3 The principle of one way of recording indicator dilution curves at the time of cardiac catheterization Dye is injected directly into the selected chamber of the heart (in this case right atrium) and its passage through the pinna of the ear recorded by a photoelectric cell device connected via an amplifier to a recorder

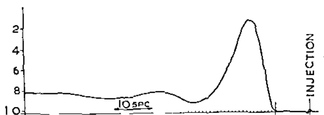


FIGURE 4 Actual dye dilution curve recorded from the pinna of the ear by a photoelectric cell and amplifier (injection into right atrium) Note appearance of first and second recirculation (Curve drawn from right to left)

electronic amplifiers has made possible the continuous recording of the passage of a dye The blood may be allowed to flow continuously through a cuvette attached to a needle in a peripheral artery On one side of the cuvette is a light source and suitable optical filter, on the other is a photoelectric cell connected via a suitable amplifier to a recorder The passage of the dye in front of the photoelectric cell causes a decrease in the current passed and deflection of the recording pen Wood and Geraci (1949) in America, Kopelman and Lee (1951) and Korner and Shillingford (1955) in this country have used the ear oximeter to record dye curves *in vivo* (Figures 3 and 4) A light source is placed on one side of the pinna of the ear and two small selenium cells on the other side A red filter is in front of one and an infrared filter in front of the other The cells are connected in electrical opposition Changes in thickness of the ear produced by arterial pulsation affect each cell equally and are neutralized The passage of dye through the ear affects only the cell with the red filter and produces an electrical current which may be amplified and recorded Providing the response of the apparatus is linear, the dye dilution curve may be calibrated by measuring the height of its tail and comparing this with the final concentration in the plasma estimated spectrophotometrically

The use of these dye dilution curves in the study of the circulation in man will now be considered

The Estimation of Cardiac Output

The principles underlying the measurement of the cardiac output by the dye technique can be compared with that of the direct Fick method

In the Fick procedure the blood flow is calculated from the formula

$$F = \frac{O}{A - V}$$

in which F is the blood flow in litres per minute O is the oxygen uptake in ml per minute, and (A – V) is the difference in oxygen content between arterial and mixed venous blood in ml per litre The assumptions required are (a) that no appreciable

amount of oxygen is taken up by the lungs, and (b) that the venous blood sample is fully mixed

With the injection method the rate of blood flow as described by Hamilton and his co workers is calculated from the relation ship

$$F = \frac{I}{CT}$$

where F is the blood flow in litres per second, I is the amount of indicator substance in mg injected into a vein, C is the average concentration (in mg /l) to which the injected substance is diluted by the blood stream during the first circulation, and T the time in seconds required for the circulation of the dye

An illustration of this relationship is shown in Figure 1 in which water is flowing through a simple model If dye is rapidly injected into the incoming stream it will mix with the water and be carried through to the outlet where it may be sampled directly The flow is directed into tubes arranged to take samples every second The rest of the stream containing dye is collected in a container If the collections in the tubes and in the container are begun with the first appearance of the dye and stopped after all the dye has passed and if the mean rate of flow is constant then the average concentration of the dye in the samples in the tubes can be shown to be the same as the concen tration of the dye in the water in the container Therefore the average concentration of the dye in the samples in the tubes provides a measure of the rate of flow For example if 12 mg of dye are injected and it takes 30 seconds for the dye to pass out of the system, and if during that time 3 litres of dyed water are collected then the 12 mg of dye will be found in the 3 litres of water, and the average concentration of dye in the sampling tubes will be 4 mg /l The rate of flow is calculated from the formula

$$F = \frac{I}{CT} = \frac{12}{4 \times 30} = 0\ 1 \text{ litres per second}$$

or 6 litres per minute the result is the same as the rate of flow measured directly from the dye concentration or from the volume of the fluid in the container

In animals or man the dye dilution curve is modified, however, by the appearance of the recirculation curve on the descending limb of the primary curve (Figure 5) Hamilton and his co workers showed that the first part of the descending limb

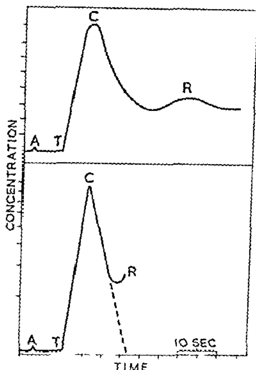


FIGURE 5 *Top* A typical indicator time-concentration curve obtained in man showing point of injection A appearance time AT peak concentration C and exponential fall-off with recirculation curve R *Bottom* The indicator dilution curve replotted on semilogarithmic paper to determine the time downslope if recirculation had not been present

before the recirculating indicator has reached the sampling site, is exponential in form and if plotted semi logarithmically, the descent is along a straight line as it is in the straight flow models Sometime later a break in this usually followed by a second rise in concentration is clearly recognizable This marks the beginning of the recirculation and the extension downward of the straight line portion of the descending limb ignoring the

secondary rise, makes possible the construction of the curve which would have obtained if the dye had not recirculated

The further assumption necessary to justify this method of calculating cardiac output is that the indicator substance mixes uniformly with the blood, and that its concentration is determined with accuracy

Several workers have made comparisons of the cardiac output obtained by the Fick method and by indicator dilution curves Hamilton, Riley Attyah, Cournand, Fowell Himmelstein, Noble, Remington Richards, Wheeler and Witham (1948) compared the difference by simultaneous determinations in 31 subjects using the intermittent sampling technique The outputs by the two methods agreed to within 25 per cent in all but six determinations The distribution of results about the line of identity was symmetrical and the authors came to the conclusion that the scatter was no greater than would be expected when known inaccuracies in both methods are considered Kopelman and Lee (1951) using the intermittent blood sampling method found similar agreement while Gilmore Hamilton Kopelman and Sommer (1954), using an ear oximeter to record the passage of the dye, found the error to be of the same order as that of Hamilton and his associates (1948)

My own experience agrees with that of previous workers The method has a decided advantage in that it offers a technique for the determination of cardiac output without the need for cardiac catheterization The ear oximeter obviates the need for arterial sampling and the determination of cardiac output may be made rapidly in the ambulant patient

The Estimation of Blood Volume between the Injection and Sampling Sites

Hamilton and his colleagues postulated that the volume of fluid through which the indicator particles had passed could be measured as a product of transit or circulation time and the speed of flow as

$$V = \frac{C\,O \times M\,C\,T}{60}$$

where V is the volume in litres C O the cardiac output in

litres per minute and M C T the mean circulation time in seconds

The interpretation of the result obtained by this method in man is difficult It includes the vessels and heart chambers actually traversed by the indicator Slow passage of the dye up the veins of the arm prolongs the appearance and mean circulation times, and tends to overestimate the central volume Injection of the indicator substance through a cardiac catheter directly into the chambers of the heart reduces this error, but *distortions of the curve may still occur as a result of uneven* mixing of the dye in its passage through the heart and lungs The interpretation of the meaning of the measurement of central volume by this method presents considerable difficulty, and time does not permit a more detailed discussion of the discrepancies that may arise It is unlikely, however, that small changes in volume can be detected with accuracy by this method

Indicator Dilution Curves Associated with Valvular Regurgitation

In the absence of valvular incompetence, the parameters of the indicator dilution curve, both in model circulations and in man, can be shown by double regression equations to be closely correlated to the cardiac output and volume as calculated from the curves (Korner and Shillingford, 1956)

The regression equation below has been made from the analysis of 71 dye curves obtained from patients with no significant valvular heart disease

$$\log \frac{1}{S} = 0\ 8799 - 0\ 061\ C\,O + 1\ 112 \log V$$

where S = the slope of the descending limb of the curve
C O = the cardiac output calculated from the curve
V = the central volume calculated from the curve

The introduction of valvular incompetence in the passage of the dye tends to alter these parameters quite apart from those predicted from the formula for output and volume The striking differences, for example between the contours of indicator

dilution curves recorded in healthy subjects and those in patients with severe disease of the mitral valve, can be seen in Figure 6 In the patient with mitral stenosis there is a generalized increase in all of the time components of the curve due

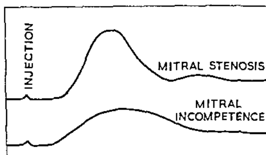


FIGURE 6 Dye dilution curves from a patient with mitral stenosis and another with mitral incompetence (see text)

to the lowered cardiac output and increased central volume associated with this condition Where severe mitral regurgitation is present, in addition to the generalized prolongation of the time components there is a disproportionate increase of the spread of the particles and prolongation of the disappearance slope

The effect of the addition of valvular incompetence can be more readily understood by considering the behaviour of the indicator particles at the incompetent valve Figure 7 represents the left atrium and left ventricle with an incompetent mitral valve If, for example the forward output from the left ventricle into the aorta is four litres per minute and the regurgitant flow through the valve the same amount, then the total left ventricular output is doubled The rate of forward flow between the left atrium and left ventricle is therefore doubled and results in an earlier appearance time of the first particles At the same time the regurgitant jet causes further mixing of the oncoming dye in the atrium and a consequent increase in the spread of the indicator dilution curve

The use of the multiple regression equation to determine the expected parameters of the curve should make it possible

theoretically to discriminate the change produced by incom petence and give a quantitative estimate of the amount of re gurgitant flow across an incompetent valve Unfortunately, it has been found that the use of this method to estimate valvular

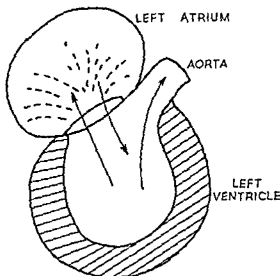


FIGURE 7 The effect of valvular incompetence on the passage of indicator particles Where *mitral incompetence is present some of the particles are* regurgitated back into the atrium to be remixed with the oncoming blood This causes increase in spread of curve The addition of valvular incom petence however causes no delay of the particles that are swept through *without being regurgitated into the atrium so that the appearance time of* the curve is not lengthened

incompetence in individual patients may be subject to a large error due to the unpredictable way in which the indicator mixes in chambers of different size and shape

Recently a simple empirical method of estimating mitral *incompetence from dye dilution curves has been investigated* (Shillingford, 1958) The spread of the curve in seconds at a fixed arbitrary fraction of the maximum concentration is divided *by the appearance time In a series of patients without valvular* incompetence the ratio obtained from these figures varied between 1 5 and 2 8 The effect of adding incompetence is to shorten the appearance time and increase the spread of the

curve, thus increasing the spread/appearance time ratio In patients with severe regurgitation the ratio may reach 15 or over The preliminary observations show a rough correlation between the clinical findings and the results given by this technique and it may prove to be a useful additional test as it is quickly and easily made without involved mathematical calculation

The correlation of the estimation of aortic regurgitation by this method and the clinical findings is not however so clear

The specific effect caused by the addition of valvular incompetence in the passage of indicator particles through the circulation has also been used to localize the site of the regurgitation in cases of congenital heart disease with multiple defects (Wright and Wood, 1957) In these patients dye is injected selectively into different chambers A normal curve will be recorded when the dye is injected distal to an incompetent valve, but an abnormal curve will be recorded from a proximal injection

Indicator Dilution Curves in Congenital Heart Disease

The introduction of an intracardiac shunt into the passage of indicator particles through the heart causes changes in the time concentration curve recorded in the systemic circulation There are two basic patterns of curve the one produced by the right to left and the other by the left to right shunt

Figure 8*a* shows the curve associated with the right to left shunt Some of the indicator particles pass through the defect and reach the sampling site earlier than normal, resulting in a shortened appearance time and distortion of the upstroke of the curve The rest of the indicator passes through the longer circuit and produces a normal type of curve

Figure 8*b* shows the effect of a left to right shunt on the behaviour of the indicator particles Some of the indicator is sequestered by the shunt and passes through the pulmonary circulation a second time This process is repeated on each subsequent circulation until all the dye has been cleared The effec- on the curve is to produce a prolongation of the descending slope of the curve and conversion of its normal exponential form into a series of small humps as each successive group of particles

leaving the pulmonary circulation arrives at the sampling site The appearance time is not altered

Although this change in the indicator curves may be used as a screening test to detect the presence of intracardiac shunts, its

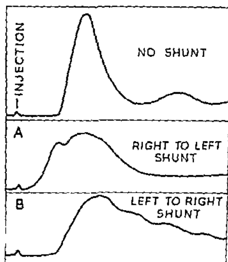


FIGURE 8 The basic patterns of indicator dilution curves associated with intracardiac shunts

practical application when the indicator is injected into the peripheral venous circulation is limited It has been demon strated however that the value of indicator dilution curves in the diagnosis of congenital heart disease may be increased by selective injection into the different chambers of the heart My own experience in this field is comparatively limited and much of what I have to say has been taken from the publications of the Mayo clinic

LOCALIZATION OF LEFT TO RIGHT SHUNTS

Figure 9 shows the use of indicator dilution curves to demon strate the presence of a left to right shunt at or distal to the left ventricle The passage of the dye injected into the left ventricle is indicated by the arrow and the corresponding dilution curve illustrated below The presence of a ventricular septal defect or

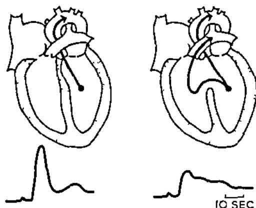


FIGURE 9 The detection of a ventricular septal defect by indicator dilution curves (see text)

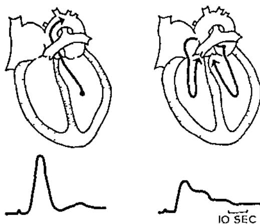


FIGURE 10 Indicator dilution curves in the presence of an atrial septal defect (see text)

aorto pulmonary shunt, produces a curve with a recirculation pattern on the downslope

In Figure 10 where there is an atrial septal defect with a left to right shunt, injection of the indicator into the left ventricle gives a normal curve, but injection into the left atrium is accompanied by the abnormal dilution curve of a left to right shunt

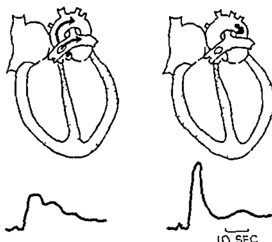


FIGURE 11 The localization of an aorto pulmonary shunt by indicator dilution curves

Figure 11 shows a valuable application of the technique in differentiating between a patent ductus arteriosus and an aorto pulmonary *fistula at the root of the aorta* These two conditions are often very difficult to differentiate by other means By successive injections through an arterial catheter under fluoroscopic control, the position of the shunt on the aortic arch may be defined Injection proximal to the fistula results in a dye dilution curve with the characteristic contour of a left to right shunt, whilst injections at all sites distal to this give normal curves

When a cardiac catheter enters the pulmonary vein it is difficult to be certain whether the vein is anomalously con nected to the right atrium *or one of its tributaries, or whether it* is normally connected to the left atrium and the catheter has

traversed an interatrial communication to enter a normally situated pulmonary vein Indicator dilution curves, made at the time of cardiac catheterization, are of value in indicating the drainage of the pulmonary vein into which the catheter has entered Where the normal venous drainage into the left atrium exists dissimilar curves between injection into the pulmonary vein and superior and inferior venae cavae will be

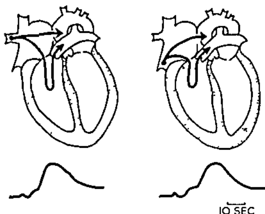


FIGURE 12 Localization of pulmonary venous drainage by indicator dilution curves (see text)

obtained If the drainage of the pulmonary vein is into the right atrium however injection into this vein will give similar curves to those obtained by injection into the superior and inferior venae cavae (Figure 12)

THE USE OF INDICATOR CURVES IN DEFINING THE OUTFLOW PATHWAYS OF THE RIGHT VENTRICLE

Ventricular septal defect may be accompanied by pulmonary stenosis or atresia and displacement of the aorta During cardiac catheterization the catheter may be passed into the left ventricle to aorta through the septal defect but it may not be possible to introduce the catheter into the pulmonary artery and so establish the presence or absence of a pulmonary outflow tract Figure 13 shows the value of indicator dilution curves in this condition Injection of dye into the aorta produces a dissimilar

curve to that produced from the left ventricle, showing that there is dye passing through the pulmonary circulation by way of the pulmonary valve

I have indicated only some of the uses of indicator dilution curves in congenital heart disease The technique lends itself to many combinations of injection and sampling sites, in the diagnosis of a difficult case

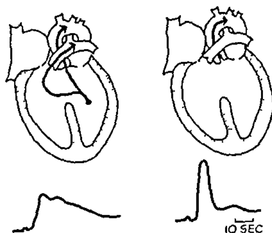


FIGURE 13 Indicator dilution curves used to confirm the presence of a pulmonary circulation (see text)

Although there is still much work to be done on the simplification and improvement of recording methods, the introduction of new indicator substances will undoubtedly extend the scope of this technique which is rapidly establishing a place in the investigation of the normal and abnormal circulation

REFERENCES

FOX I J and WOOD E H (1957) *Proc Mayo Clin* 32 541

GILMORE H R HAMILTON M KOPELMAN H and SOMMER L S (1954) *Brit Heart J* 16 301

HAMILTON W F MOORE J W KINSMAN J M and SPURLING R G (1932) *Amer J Physiol* 99 534

HAMILTON W F RILEY R L ATTYAH A M COURNAND A FOWELL D M HIMMELSTEIN A NOBLE R P REMINGTON J W RICHARDS D W JR WHEELER N C and WITHAM A. C (1948) *Amer J Physiol* **153** 309
HERING E (1829) *Ztschr Physiol* **3** 85
KOPELMAN H and LEE G DE J (1951) *Clin Sci* **10** 383
KORNER P I and SHILLINGFORD J P (1955) *Clin Sci* **14** 553
KORNER P I and SHILLINGFORD J P (1956) *Clin Sci* **15** 417
SHILLINGFORD J P (1958) *Brit Heart J* In press
STEWART C H (1894) *J Physiol* **15** 1
WOOD E H and GERACI J E (1949) *J Lab clin Med* **34** 387
WRIGHT J L and WOOD E H (1957) *Proc Mayo Clin* **32** 491

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